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Neuroergonomics Deep Dive Literature Review, Volume 1: Neuroergonomics and Cognitive State

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14. ABSTRACT
This report is the first of two volumes summarizing published papers that were reviewed broadly within the area of neuroergonomics, with a specific focus on Air Force interests. The included references are not intended to be exhaustive, but rather to include review articles and representative empirical papers by the key researchers in each topic, thus providing a solid basis for understanding the state of this research.

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Neuroergonomics and Cognitive State

Contents

Executive Summary

Neuroergonomics is a term coined by Professor Raja Parasuraman, first introduced in his 2003 publication and expanded by the 2007 book of the same name. In his definition, neuroergonomics is the study of brain and behavior at work". This particular focus on work and applications distinguishes neuroergonomics from the broader field of neuroscience; likewise, it is distinguished from traditional human factors and ergonomics by the emphasis on neuroscientific approaches and methods. Work that could be described as neuroergonomic certainly predates the introduction of the term. Parasuraman is explicit in stating his goal to promote work of this type among the neuroscience community and advance broader acceptance of neuroergonomic techniques in the human factors community, and even speculates that the term may be abandoned at such point as this goal is accomplished.

From the perspective of the Air Force Research Laboratory (AFRL), neuroergonomics is an area of particular interest for many reasons. Work in this area offers tremendous transformative potential in human performance augmentation, and with the application-oriented thrust neatly aligns with U.S. Air Force "technology push" goals as articulated in the Technology Horizons (2010) report. AFRL researchers have already made some significant contributions to neuroergonomic research. Two of the chapters in the 2007 book were authored by AFRL scientists in addition to coauthorship with Professor Parasuraman on numerous journal articles. That said, with turnover in the personnel performing this work neuroergonomics was identified as needing additional focus. The Neuroergonomics Deep Dive was therefore initiated to scope out appropriate goals for AFRL work in the area and build a truly world-class reputation.

In order to identify AFRL goals, criteria were established by the Deep Dive team. These include the following:

1. The research must be applicable to Air Force selection, operations or training.
2. It must be neuroergonomic in character, blending neuroscience and human factors.
3. Work that is already well-covered outside AFRL should be monitored and leveraged, not duplicated in-house.

As a preliminary to setting goals for AFRL research, a literature review was undertaken by a team of scientists from across the Human Effectiveness Directorate. The intent of this review was to identify existing research topics that meet the above criteria, as well as revealing underserved or emerging topics worthy of consideration. Eleven topics have been identified and reviewed. This report in two volumes summarizes the literature that was reviewed by topic. The listed references are not intended to be exhaustive, but rather to include review articles and representative empirical papers by the key researchers in each topic, thus providing a solid basis for understanding the state of this research.

Acknowledgements

The authors would like to gratefully acknowledge Kathryn Sidrow and Kyle Traver for their assistance in editing and formatting the chapters of this report. We would also like to acknowledge Drs. Joel Warm and Lloyd Tripp for their input as advisors on this project. Lastly, we thank Dr. Morley Stone for his support and for originating the current focus on this area at AFRL.

Chapter 1

Introduction

Why Neuroergonomics?

At less than ten years old, the term neuroergonomics is likely still unfamiliar to many. With the proliferation of neuro- terms in recent years, a very reasonable question is to ask why exactly this term is necessary and what value it adds to the research enterprise. The term of course represents an idea: the tremendous progress and investment in neuroscience can and should be focused on specific work environments in order to produce significant augmentation of human performance. In so doing, the intent is to motivate researchers in both neuroscience and human factors to expand their viewpoint, increase collaboration, and accelerate the development of neuroscientific technology. Inasmuch as the term is successful at generating attention and focused funding opportunities it adds tremendous value.

Neuroergonomics is also distinguished from neuroscience more generally by funding agency priorities. In 2005 the National Institute of Health (NIH) provided approximately $5.9B, or 42% of all neuroscience funding, with particular focus on neurological disorders, mental health, substance abuse, and aging. Pharmaceutical firms provided $7B, or 50%[1]. It is unsurprising that as a result, most of the semi-applied research being conducted is focused on understanding and treatment of pathological states. Research focused on maintaining or enhancing otherwise healthy humans, the key focus for neuroergonomics, has received comparatively little attention in the broader research community.

Neuroergonomics and the Department of Defense

Department of Defense (DoD) agencies have a significant and likely preeminent role in what funding has been provided that has sought to advance the application of neuroscience research in normal work domain, stemming naturally from DoD interest in enhanced warfighting capabilities. The Defense Advanced Research Projects Agency (DARPA) has funded work via programs such as Augmented Cognition and Neurotechnology for Intelligence Analysts, the Army Research Laboratory (ARL) has funded the Cognition and Neuroergonomics Collaborative Technology Alliance, and the Air Force Research Laboratory (AFRL) has funded the Center for Excellence in Neuroergonomics, Technology, and Cognition. While there are many unique aspects to each of these efforts, they share a common interest in promoting neuroergonomic research.

AFRL has several strengths that make the organization well-suited to a focus on neuroergonomic research. In addition to collaborating on many of the foundational works in the area from 2003 on, work of this type has been performed at AFRL since at least the late 1980s[2]. AFRL has a tradition of building interdisciplinary research teams capable of performing

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NB: Papers appearing in the summaries are referenced parenthetically; those not summarized are footnoted.

[1] Dorsey, E.R., Vitticore, P., De Roulet, J., et al. (2006). Financial anatomy of neuroscience research. *Annals of Neurology,* 60, 652–659.

[2] e.g, Papanicolaou, A.C., Wilson, G.F., Busch, C., et al. (1988). Hemispheric asymmetries in phonological processing assessed with probe evoked magnetic fields. *International Journal of Neuroscience,* 39(3-4):275-81.

complex, technically challenging in-house work, and the ability to maintain these teams and funding in comparatively stable fashion. The expense and technical sophistication required for top-quality neuroergonomic research makes this essential. With some key AFRL personnel retiring or moving on to jobs beyond the bench level as well as the incredible breadth of work being conducted in neuroscience, the need has arisen to focus on neuroergonomics in an effort to identify specific goals for AFRL work and enhance our standing in this area. In response to this, AFRL has initiated the Neuroergonomics Deep Dive.

The Neuroergonomic Deep Dive

As the title suggests, the Neuroergonomic Deep Dive was created to deeply immerse AFRL scientists in neuroergonomic research in order to survey the field, create ideas, and plan future work. The end products of this effort range from high-level research goals to funding, personnel, and equipment projections. To this end, a team was assembled consisting of members from across the AFRL Human Effectiveness Directorate. This team mapped out actions to accomplish the goals of the deep dive, starting with conducting the literature review that this report summarizes. Following completion of the initial phase of work on this review, the deep dive has conducted two workshops to discuss our work and plans for the area. The first was an interservice workshop hosted at AFRL that brought together scientists from the Navy, Army, and Air Force to present research in the area, discuss challenges and goals, and identify new opportunities for collaboration. The second workshop was an open session at the Applied Human Factors/1st International Conference in Neuroergonomics that brought in external participants from more than 25 universities and research companies to discuss research priorities and provide external review of our progress. The deep dive is anticipated to conclude with delivery of this document, a roadmap for the next five years of work in the area, and funding, personnel, and equipment projections.

Topic Selection for Review

Even within the narrower field of Neuroergonomics, not all topics are appropriate for in-house AFRL work. In order to identify work that should be reviewed, inclusion criteria were established by the deep dive team. These include the following:

1. The research must be applicable to Air Force selection, operations or training.
2. It must be neuroergonomic in character, blending neuroscience and human factors.
3. Work that is already well-covered outside AFRL should be monitored and leveraged, not duplicated in-house.

These criteria have led to eleven topical areas being selected for review. Five will be presented in this volume, with the remainder in the second. In total, over 300 papers are summarized in the two volumes of this report.

Stress and resilience is the first area to be reviewed. It is difficult to imagine an Air Force activity that does not produce significant stress on the individuals involved. In both the short and the long term, stress produces significant decrements in human performance. As a result, understanding the neurophysiological mechanisms that underlie stress responses and stress resilience is of significant interest and decidedly neuroergonomic research. As with other neuroscience research, there is significant work outside AFRL focused on stress

pathologies such as post-traumatic stress disorder; the promising niche for AFRL work is then to study resilience and hardiness to stress in order to improve performance under stress as well as reduce the incidence of long-term negative effects.

Emotion and the effects of emotion on cognitive performance is the second area. As with stress, challenging Air Force activities will inevitably produce strong emotions; while this is usually thought of as interfering with performance, some emotional responses may actually be facilitory. Such responses produce neurophysiological changes that are detectable using neuroergonomic techniques; the key questions are then to determine how best to enhance performance with emotion regulation, and how to integrate emotional state sensing with other, closely related neurophysiological states such as stress, fatigue, and the vigilance decrement.

Vigilance, the third area, refers to the ability of observers to detect transient and infrequent signals over long periods of time. Many types of Air Force operations exhibit these characteristics; for example, an Air Force sensor operator who has been tasked with monitoring a particular building to watch for a specific individual is performing a task that requires vigilance. There have been several promising studies to date that have suggested that a decrement in vigilance is associated with neurophysiological changes that are detectable with neuroergonomic techniques; however significant work remains to better establish the relationship between performance and sets of physiological measures, as well as integrate effective countermeasures. While vigilance research is done around the world, AFRL has established expertise in the area and demonstrated capability for doing world-class vigilance research.

The fourth topic is trust, or more specifically the neuroergonomic assessment of trust. Trust may be operationally defined as being willing to place oneself in a position of vulnerability to the actions of another. Trust is another ubiquitous feature of Air Force operations, both in the sense of trusting teammates and partners as well as trusting the systems that are used. Trust unto itself is a relatively new area of research – sufficiently so to have an AFRL deep dive focused just on trust. This area is therefore a shared piece between the trust and neuroergonomic deep dives, specifically focused on the idea that trust may be detectable using neuroergonomic measures. This is also a very new idea, sufficiently so to have caused the Intelligence Advanced Research Projects Activity (IARPA) to construct a program focused squarely on the issue, in large part due to a lack of active work in the area. AFRL research in this topic will form a portion of the IARPA trust research portfolio.

The last topic covered in this volume is non-invasive brain stimulation, specifically for the enhancement of learning and cognition. The basic idea that brain function may be altered via the application of electrical current or strong electromagnetic fields is relatively old, but applications to date such as electroconvulsive therapy have focused on large doses of whole brain stimulation that produce seizure-like activity or temporary incapacitation of a brain region. The field is currently undergoing a revolution with early findings suggesting that low, subthreshold levels of stimulation may produce significant enhancement in learning speed and performance. Much research remains to elucidate the exact mechanism of action producing these enhancements, as well as how best to deliver and use the technology. This area aligns squarely with the need for human performance augmentation as identified in Tech Horizons (2010); increased performance or decreased learning time may ultimately translate

into reduced manning requirements for Air Force training and operations. As may be expected, ethical and political considerations are significant for this area and tend to limit research activity not performed or supported by the DoD.

In closing, it is important to stress that this literature review is not intended to be exhaustive; rather, it is intended to provide an annotated bibliography that covers the overall state-of-the-art in each of these research areas, and in so doing place AFRL research within the context of the larger research community. Neuroergonomics has the potential to enable incredible capabilities of significant interest to the Air Force, encompassing a full range of techniques and analysis from the molecular level to groups of individuals working together; realizing this potential will require sustained focus and investment in this work.

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Chapter 2

Stress: Hormones and Resilience

Stress is a response to a real or perceived threat that creates a cascade of psychological and physiological consequences. The effects of stress influence every body system and can range from mild learning and behavioral changes to severe psychological illness to physical diseases such as hypertension and diabetes[3]. The magnitude of the stress response can depend on a variety of factors including the situation encountered, previous stress exposure, duration and intensity of the stressor[4]. Mild stress may provide beneficial inoculating effects, while severe and chronic stress can be detrimental. In studying stress there are several factors to consider, including the type of stressor encountered, the body's physiological response, and the individual's level of resilience to adapt to the challenge.

Both human and animal research data provide insight into a variety of behavioral and biological processes that govern the individual's response to stress. Stress research in animal models can be accomplished through using physical, emotional or social stressors to mimic situations that humans encounter on a daily basis. Following a stressful encounter, the Hypothalamic Pituitary Adrenal (HPA) axis is activated, which triggers a chain reaction that ultimately results in the release of glucocorticoids (GCs) from the adrenal glands (McEwen & Sapolsky, 1995). Small quantities of GCs can help overcome a stressor by sharpening mental acuity and diverting energy to the body systems that need it most. The HPA axis is a negative feedback loop to limit GC secretion; however during times of prolonged stress, the body can become overloaded with GCs, which causes a wide array of deleterious physical and cognitive effects.

Resilience to stress is of particular military interest due to the inherent stress of military life. The negative effect of stress on military members is clearly evidenced by the rate of alcohol abuse[5], PTSD[6], and suicide[7]among returning deployed personnel. However, a large number of military members under the same stressors and condition emerge from these situations without any serious signs of distress. Resilience in the face of a stressful situation depends on a wide variety of factors including personality traits, social support, effective coping skills, and previous successful experiences with stress. Specific genetic polymorphisms that affect neurochemical and hormonal production have also been associated with an individual's response to stress and

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[3] Sapolsky, R., M., (1992). "Stress, the aging brain, and the mechanisms of neuron death". MIT Press.

[4] Larsson, F., Winblad, B., Mohammed, A.H., (2001). "Psychological stress and environmental adaption in enriched vs impoverished housed rats". *Pharmacology, Biochemistry, and Behavior*. **73**: 193-207

[5] Wilk, J.E., Bliese, P.D., Kim, P.Y., Thomas, J.L., McGurk, D., & Hoge, C.W., (2010) "Relationship of combat experiences to alcohol misuse among U.S. soldiers returning from the Iraq war". *Drug and Alcohol Dependence*. **108**: 115-121

[6] Hoge, C.W., Castro, C.A., Messer, S.A., McGurk, D., Cotting, D.I., & Koffman, R.L., (2004). "Combat Duty in Iraq and Afghanistan, Mental Health Problems, and Barriers to Care." *New England Journal of Medicine*. **351**:13-22

[7] "Army Suicide Event Report." Suicide Risk Management and Surveillance Office, 2007.

their predisposition to psychological disorders such as PTSD and major depression (Gillespie, Phifer, Bradley, & Ressler, 2009).

Another way to study resilience is to measure one of its phenomena: hardiness. Hardy individuals are more resilient against stress, as they have a strong sense of commitment to life and work and are actively engaged in their environment. They believe they can control or influence what happens, and they enjoy new situations and challenges (Bartone, Roland, & Picano, & Williams, 2008). Research suggests hardiness is trainable (Maddi, 2007); therefore it could be used to enhance the ability to handle stress.

The articles below provide insight into the psychological and physiological responses to stress, as well as the genetic variations that influence the stress response, stress resilience and hardiness.

Stress

1. **Gold, P.W., & Chrousous, G.P., (2002). "Organization of the stress system and its dysregulation in melancholic and atypical depression: high vs. low CRH/NE states."** ***Molecular Psychiatry, 7*** **(1), 254-275.**

This review paper details the stress response and how it not only is involved with depression and anxiety, but is also linked to heart disease, osteoporosis, diabetes, and other adverse medical conditions.

2. **Pijlman, F.T.A., Wolterink, G., & Van Ree, J.M., (2001). "Physical and emotional stress have differential effects on preference for saccharine and open field behavior in rats."** ***Behavioural Brain Research, 139*****, 131-138.**

This study used cage mates to test the effects of different types of stress on cognitive function. Cage mates were tested together, with one rat exposed to a physical stressor (random foot shocks), while the other was emotionally stressed by being present while the event takes place. Emotionally stressed animals were found to be more ambulatory than control and physical stress animals, and also had greater sensitivity to reward, suggesting that different types of stress affect behavior in different ways.

3. **Adamec, R., Walling, S., & Burton, P., (2004). "Long lasting, selective, anxiogenic effects of feline predator stress in mice."** ***Physiology and Behavior, 83*****, 401-410.**

This predator stress study subjected three groups of mice to varying degrees of exposure to a cat. One group was simply handled, one group was exposed to a room where a cat had been in the previous hour, and one group was placed in a room with a cat. Behavioral tests showed lasting effects were seen especially in risk assessment in both the predator exposed and odor exposed group. Predator stress studies can simulate PTSD, making them of particular military interest.

4. **Zelena, J.H.,Halasz, J., & Makara, G.B., (1998). "Social Stress of variable intensity: Physiological and behavioral consequences."** ***Brain Research Bulletin, 48,*** **(3): 297-302.**

Social stress can be carried out by exposing a rat to an aggressive rat. In this experiment, four groups were exposed to a dominant rat for 1 of 4 time periods for four days. Animals exposed to the dominant rat for only 30 minutes daily showed behavioral changes but did not show signs of chronic stress. Animals exposed for 4 hours each day developed chronic stress symptoms, suggesting duration of the encounter plays a role in stress outcomes.

5. **Van Praag, H., Kempermann, G., & Gage, F.H., (2000). "Neural consequences of environmental enrichment."** ***Nature Reviews, 1,*** **191-198.**

Environmental enrichment is a form of mild stress that can cause a variety of anatomical and electrophysical changes in the brain. Enrichment has been shown to provide cognitive benefits such as improved learning and memory. This review explains the benefits of environmental enrichment in light of a variety of conditions including brain injury and advanced age.

6. **Yerkes, R.M., & Dodson, J.D., (1908). "The Relation of strength of stimulus to rapidity of Habit formation."** ***Journal of Comparative Neurology and Psychology, 18*****, 459-482.**

This study assessed the effect of stress intensity on performance. Results showed that performance under stress corresponds to an inverted U curve; stress can improve performance to a certain point, however excessive stress is detrimental to performance.

Hormones

1. **Doczy, E.J., Seroogy, K., Harrison, C.R., & Herman, J.P., (2009). "Hypothalamo-pituitary-adrenocortical axis, Glucocorticoids, and neurological disease."** ***Immunology and Allergy Clinics of North America, 29,*** **265-284.**

This article discusses the role of limbic structures in regulating the HPA axis, GC signaling and regulation of the HPA axis as a negative feedback loop. The relationship between GCs and neurological disease are also discussed.

2. **Herman, J.P., & Cullinan, W.E. (1997). "Neurocircuitry of stress: central control of the hypothalamo-pituitary-adrenocortical axis."** ***Trends in Neurosciences, 20*** **(2), 78-84.**

Two different pathways of stress response and the role of the paraventricular nucleus in regulating the HPA axis are discussed. It is suggested that inappropriate regulation of the stress system can contribute to a variety of affective, systemic, and neurodegenerative diseases.

3. **Sapolsky, R. M. (1999). "Glucocorticoids, stress, and their adverse neurological effects: relevance to aging."** ***Experimental Gerontology, 34*** **(6), 721-732.**

This review article discussed the possible damage that can be caused by glucocorticoids. Glucocorticoids are beneficial in response to acute stress, but excessive secretion can cause a variety of neurological effects ranging from reversible cognitive deficits to neurotoxicity, neuron cell death, and hippocampal volume loss.

4. **McEwen, B.S., & Sapolsky, R.M., (1995). "Stress and Cognitive Function."** ***Current Opinion in Neurobiology, 5*****, 205-216.**

This article reviews the negative short and long term effects of glucocorticoids on cognitive and physiological processes. Stress induced learning and memory deficits are discussed, as well as possible mechanisms responsible for disrupted long term potentiation seen as a result of chronic stress. Findings from both human and animal studies are discussed.

5. **Shors, T.J., Gallegos, R.A., & Breindl, A. (1997). "Transient and persistent consequences of acute stress on long-term potentiation (LTP), synaptic efficacy, theata rhythms and bursts in area CA1 of the hippocampus."** ***Department of Psychology and Program in Neuroscience, 26*****, 209-217.**

This study evaluated the effect of stress on long-term potentiation (important in memory formation). Rats were subjected to restraint and shock stress, and then were surgically implanted with electrodes designed to monitor brain activity. LTP was found to be significantly impaired (by 50%) by acute stress for up to 48 hours after the stress.

6. **Sorrells, S,F., Caso, J,R., Munhoz, C, D., & Sapolsky, R, M. (2009). "The Stressed CNS: When glucocorticoids aggravate inflammation."** ***Neuron, 64*****, 33-39.**

This article reviews the effect of acute and chronic glucocorticoid exposure on the immune system, inflammatory response, and the injured and uninjured brain.

7. **McEwen, B. S., (1999). "Stress and hippocampal plasticity."** ***Annual Review Neuroscience*****,** ***22*****, 102-122.**

This article discusses the role of glucocorticoids, excitatory amino acids and NMDA receptors in temporary and permanent brain atrophy. Structural changes in the hippocampus, neurogenesis, and the cognitive implications are reviewed.

8. **Magarinos, A.M., & McEwen, B.S., (1995). "Stress-induced atrophy of apical dendrites of hippocampal CA3c neurons: Involvement of glucocorticoid secretion and excitatory amino acid receptors."** ***Neuroscience, 69*** **(1), 89-98.**

This paper investigated a method to prevent stress induced brain atrophy as a result of corticosterone. In this experiment, rats underwent chronic restraint stress, with experimental groups receiving an injection of cyanoketone, which inhibits corticosterone in the stress response. Results showed cyanoketone treatment prior to restraint stress prevented stress induced atrophy in the CA3 region of the brain.

9. **Kim, J. J., & Diamond, D.M., (2002). "The stressed hippocampus, synaptic plasticity and lost memories."** ***National Review Neuroscience, 3*** **(6), 453-462.**

This article discusses the hippocampus/CA3 region‘s role in learning and memory processes and HPA axis regulation. The brain and hippocampus‘ sensitivity to stress is explained as a result of the hippocampus containing the largest number of corticosteroid receptors in the brain, making it especially vulnerable to the deleterious effects of excessive Glucocorticoids.

10. **Ozbay F., Fitterling H., Charney D., & Southwick S. (2008). "Social support and resilience to stress across the life span: A neurobiologic framework."** ***Current Psychiatry Reports, 10*****, 304-10.**

This article suggests psychologically resilient people maintain their sympathetic nervous system activation within an optimal window – high enough to respond to danger but not so high as to produce incapacitating anxiety and fear. Several neurochemicals (NPY, galanin, cortisol, oxytocin, vasopressin) are discussed regarding their effect on anxiolysis and performance. The author supports a common idea throughout the literature that stress inoculation confers stress resistance via brief, well-contained activations of the HPA axis which may in turn optimize the neuroendocrine response to stress and enhance coping-oriented behavior.

Resilience

1. **McEwen, B.S., (1998). "Stress, adaptation and disease."** ***Annals New York Academy of Sciences, 840*****, 33-44.**

This paper discussed the concept of allostatic load; the consequence of and lack of adaptation to chronic stress. Topics reviewed include the impact of stress on the brain, including decreased hippocampal function and memory deficits, the importance of adaptation to stress and individual differences that moderate adaptation, and the relationship between chronic stress and immune system function.

2. **Parker, K.J., et al. (2004). "Prospective investigation of stress inoculation in young monkeys."** ***Archives of General Psychiatry, 61*****, 933-941.**

This study showed that monkey's stressed as juveniles showed diminished anxiety in a novel situation as adolescents. Young monkeys separated from their mothers on a weekly basis showed diminished signs of stress weeks later when confronted with a novel environment. The monkeys with previous stress experience showed fewer signs of anxiety than control groups, suggesting that an unrelated previous stressful experience had a stress inoculating effect.

3. **Frisone, D.F., Frye, C.A., & Zimmerberg, B., (2001). "Social Isolation stress during the third week of life has age-dependent effects on spatial learning in rats."** ***Behavioral Brain Research, 128,*** **153-160.**

Rats are highly social animals, and the simple act of keeping them in a cage alone is enough to cause emotional stress. This study isolated juvenile rats for 6 hours daily for seven days, followed by 3 days of Morris Water Maze (MWM) testing to measure short term memory and spatial learning. Results showed the isolated animals performed poorly on the task as juveniles, however performed better when tested as adults. This suggests that the learning and spatial memory deficits observed were reversible and that mild stress in early life can improve cognitive performance when face with stressors later in life.

4. **Knight, G.K., Gatz, M., Heller, K., & Bengtson, V.L., (2000). "Age and emotional response to the northridge earthquake: A Longitudinal Analysis."** ***Psychology and Aging, 15*** **(4), 627-634.**

The concept of stress inoculation as a source of resilience was explored in a study following the 1994 Northridge earthquake. This telephone study interviewed adults who experienced the Northridge quake and found that those who had lived through previous earthquakes were less

depressed than those who did not have that experience. These findings suggest that stress inoculation from previous experience played a role in their resilience.

5. **Pietrzak, R, H., Johnson, D, C., Goldstein, M, B., Malley, J, C., & Southwick, S, M. (2009). "Psychological resilience and post deployment social support protect against traumatic stress and depressive symptoms in soldiers returning from operations enduring freedom and Iraqi freedom."** ***Depression and Anxiety, 26*****, 745-751.**

This study asked OIF/OEF veterans to complete a series of surveys regarding their deployment experience, perceived social support, and personal traits. Results showed that PTSD was inversely correlated with social support, suggesting that social support is a key aspect of resilience in traumatic situations.

6. **Bonanno, G. A. (2005). "Resilience in the face of potential trauma. Current Directions."** ***Psychological Science, 14,*** **135-138.**

This article gives an overview about recent research indicating that the most common reaction among adults exposed to traumatic events is a relatively stable pattern of healthy functioning coupled with the enduring capacity for positive emotion and generative experiences. There appear to be multiple and sometimes unexpected ways to be resilient, and sometimes resilience is achieved by means that are not fully adaptive under normal circumstances.

7. **Bonanno, G. A. (2004). "Loss, trauma, and human resilience: Have we underestimated the human capacity to thrive after extremely adverse events?"** ***American Psychologist, 59,*** **20-28.**

The author of this highly cited paper reviews evidence that resilience represents a distinct trajectory from the process of recovery, that resilience in the face of loss or potential trauma is more common than is often believed, and that there are multiple and sometimes unexpected pathways to resilience.

8. **Fredrickson, B. L., Tugade, M. M., Waugh, C. E., & Larkin, G. R. (2003). "What good are positive emotions in crisis? A prospective study of resilience and emotions following the terrorist attacks on the United States on September 11th, 2001."** ***Journal of Personality and Social Psychology, 84*** **(2), 365-376.**

U.S. college students (18 men and 28 women) were tested in early 2001 and again in the weeks following the September 11th terrorist attacks. Mediational analyses showed that positive emotions experienced in the wake of the attacks— gratitude, interest, love, and so forth—fully accounted for the relations between (a) pre-crisis resilience and later development of depressive symptoms and (b) pre-crisis resilience and post-crisis growth in psychological resources. Findings suggest that positive emotions in the aftermath of crises buffer resilient people against depression.

9. **Bonanno, G. A., Galea, S., Bucciarelli, A., & Vlahov, D. (2006). "Psychological resilience after disaster: New York City in the aftermath of the September 11th Terrorist Attack."** ***Psychological Science*****,** ***17,*** **181-186.**

This study examined the prevalence of resilience, defined as having either no PTSD symptoms or only one symptom, among a large (n = 2,752) probability sample of New York area residents during the 6 months following the September 11th terrorist attack. Resilience was observed in 65.1% of the sample and more than half of the people who saw the attack in person or experienced the death of a friend or relative in the attack were resilient.

10. Masten, A. S. (2001). "Ordinary magic: Resilience Process in development." ***American Ppsychologist, 56,*** **227- 238.**

The study of resilience in development has overturned many negative assumptions and deficit-focused models about children growing up under the threat of disadvantage and adversity. The most surprising conclusion emerging from studies of these children is the ordinariness of resilience. The conclusion that resilience is made of ordinary rather than extraordinary processes offers a more positive outlook on human development and adaptation, as well as direction for policy and practice aimed at enhancing the development of children at risk for problems and psychopathology.

11. Luthar S, S., & Cicchetti, D., & Becker, B. (2000). "The Construct of Resilience: A Critical Evaluation and Guidelines for Future Work." ***Children Development. 71*** **(3), 543–562.**

This article presents a critical appraisal of resilience, a construct connoting the maintenance of positive adaptation by individuals despite experiences of significant adversity. As empirical research on resilience has burgeoned in recent years, criticisms have been levied at work in this area. This paper address each identified criticism in turn, proposing solutions for those the authors view as legitimate and clarifying misunderstandings surrounding those they believe to be less valid.

12. Mansdorf, I, J., (2008). "Psychological interventions following terrorist attacks." ***British Medical Bulletin, 88,*** **7–22.**

A review of representative studies is presented, with a critical analysis of the salient points of the various psychological intervention strategies for terrorist attacks. The author shows, if the debriefing mechanism is refined so that intrusive emotional rehashing of the traumatic event is eliminated, the resultant interventions resemble resilience based approaches.

Hardiness

1. Maddi, S,R., (2007). "Relevance of Hardiness Assessment and Training to the Military Context." ***Military Psychology, 19*** **(1), 61 – 70.**

This article starts with a summary about theory and research on hardiness assessment and training, then highlights relevance to stressful situations. Likely applications of hardiness assessment and training in particular military contexts, such as selection and preparation for Special Forces or other extreme assignments, are discussed as well.

2. Adler, A, B., & Dolan, C, A., (2006). "Military hardiness as a buffer of psychological health on return from deployment." ***Military Medicine, 171*****, 93-98.**

In this survey study of 629 U.S. soldiers, deployment stressors, military hardiness, and psychological and physical health were assessed during a peacekeeping deployment. The results show that military hardiness moderated the impact of deployment stressors on depression after deployment.

3. **Bartone, P,T., Roland, R, R., Picano, J, J. & Williams, T, J. (2008). "Psychological Hardiness Predicts Success in US Army Special Forces Candidates."** ***International Journal of Selection and Assessment, 16*** **(1), 78-81.**

In this study US Army Special Forces candidates (N=1138) were assessed for psychological hardiness using a short form of the Dispositional Resilience Scale, and these scores were then applied to predict successful completion of the course. Analyses confirmed that Special Forces course graduates are significantly higher in psychological hardiness as compared to non-graduates. Psychological hardiness appears to be an important individual characteristic associated with stress tolerance and successful performance in highly demanding occupations.

4. **Bartone, P, T. (2006). "Resilience under military operational stress: Can leaders influence hardiness?"** ***Military Psychology, 18,*** **131-148.**

This study examined traits in military leadership to ascertain if leadership style or qualities had an effect on hardiness in a military setting. Results showed that hardiness was viewed most favorably as a quality in military leaders, and that hardy leaders may be able to influence subordinate hardiness as well.

5. **Bartone, P, T., (1999). "Hardiness protects against war-related stress in Army reserve forces."** ***Consulting Psychology Journal*****,** ***51*** **(2), 72-82.**

A survey study of Army Reservists found that those with hardy personalities were less likely to experience psychological symptoms following combat exposure. A proposed mechanism for this is that hardy individuals are more likely to create strong social networks and find a sense of purpose in their work, even when it is very stressful. This aids in coping with work related stresses, and is a possible mechanism for why PTSD in returning veterans is lower among those with strong social support.

6. **Bartone, P, T., (1989). "Predictors of Stress-Related Illness in City Bus Drivers."** ***Journal of Occupational and Environmental Health, 31*** **(8), 657-663.**

This study examines the relationship between stress and illness among bus drivers in a large American city. Four variables were identified that differentiate bus drivers who get ill under high stress (N = 137) from those who remain healthy under stress (N = 137). Highly stressed and ill bus drivers use more avoidance coping behaviors, report more illness in their family medical histories, are low in the disposition of "personality hardiness," and are also low in social assets.

7. **Britt, T.W., Adler, A.B., & Bartone, P.T., (2001). "Deriving benefits from stressful events: The role of engagement in meaningful work and hardiness."** ***Journal of Occupational Health Psychology, 6*** **(1), 53-63.**

This research (Participants US-Soldiers N=161) explored the relationship between the meaningfulness of work, personality hardiness, and deriving long-term benefits from a stressful event. The authors showed that personality hardiness was related to the tendency to find meaning in work during the deployment as evidenced by the soldiers identifying with the peacekeeper role, believing their job on the mission was important, and being personally engaged in the mission, which was strongly associated with deriving benefits from the deployment months after it was over. Enriching experiences were also associated with deriving benefits from the deployment.

8. **Florian, V., Mikulincer, M., & Taubman, O., (1995). "Does hardiness contribute to mental health during a stressful real-life situation? The roles of appraisal and coping."** ***Journal of Personality and Social Psychology, 68*** **(4), 687-695.**

In this study Israeli recruits (N = 276) completed questionnaires on hardiness, mental health, cognitive appraisal, and ways of coping at the beginning and end of a demanding, 4-month combat training period. Path analysis revealed that two components of hardiness—commitment and control measured at the beginning of the training—predicted mental health at the end of the training through the mediation of appraisal and coping variables. The present findings seem to provide highly valuable information to the conceptualization of hardiness as a stress-resistance resource.

9. **Vogt, D,. Rizvi, S, R., Shipherd, J, C., & Resick, P, C., (2008). "Longitudinal investigation of reciprocal relationship between stress reactions and hardiness."** ***Personality and Social Psychology Bulletin, 34*** **(1), 61-73.**

In this longitudinal study of 1,571 Marine recruits who participated in a highly stressful training program, the authors applied regression-based cross-lagged analyses to examine associations between stress reactions and hardiness over time for both men and women, and they investigated social support as a moderator of these relationships. Men who were hardier at Time 1 (T1) reported lower stress reactions at Time 2 (T2), and men who experienced more stress reactions at T1 were less hardy at T2.

Genetics

1. **Feder, A., Nestler, E.J., & Charney, D.S. (2009). "Psychobiology and molecular genetics of resilience."** ***Nature Reviews Neuroscience, 10*** **(6), 446-57.**

This article reviews the concept of resilience and how it is affected by behavioral, genetic, neurochemical, neuroendocrine and neural system components. Polymorphisms in Corticotrophin Releasing Hormone (CRH), serotonin, catechol-O-methyltransferase (COMT) and BDNF genes are discussed as well as their differential phenotypes in response to stress. Epigenetic mechanisms of resilience are discussed as well.

2. **Ising, M., & Holsboer, F. (2006). "Genetics of stress response and stress-related disorders."** ***Dialogues Clinical Neuroscience, 8*** **(4), 433-44.**

This article reviews several genes that affect the psychosocial stress response. The identified genes affect at least the cortisol response to psychosocial stress and include glucocorticoid receptors, GABA receptors and opioid receptors.

3. Moffitt, T.E., Caspi, A., & Rutter, M. (2006). "Measured gene-environment interactions in psychopathology." ***Perspectives on Psychological Science, 1*** **(1), 5-27.**

This article summarizes the Gene X Environment interaction theory and reviews polymorphisms known to affect risk of psychiatric disorders following exposure to a given environment. Genes associated with variations in phenotype due to environments such as cannabis use, bacterial infection, dietary fat intake and head injury were discussed. In most cases, it was noted that the gene bore no significant relation to health outcome in the absence of exposure to an environmental pathogen.

4. Rutter, M. (2006). "Implications of resilience concepts for scientific understanding." ***Annals New York Academy of Sciences, 1094,*** **1-12.**

This review article discusses resilience and emphasizes that, instead of a universally applicable resilience trait, resilience is affected by specific Gene X Environment interactions and that traits associated with resilience have little or no effect on psychopathology in the absence of the environmental risk factor. The author urges researchers to evaluate resilience in relation to specific environmental hazards and over a life-span since specific adult experiences may be affected by positive or adverse childhood experiences.

5. Belsky, J., Jonassaint, C., Pluess, M., Stanton, M., Brummett, B., & Williams, R. (2009). "Vulnerability genes or plasticity genes?" ***Molecular Psychiatry,*** **14 (8), 746-54.**

This article presents an interesting finding that particular genotypes may make individuals disproportionately vulnerable to adversity but may also confer on them an advantage when it comes to benefiting from an enriched environment. Individuals with a less active version of the monoamine oxidase A (MAOA) gene were more likely to become antisocial and have ADHD if maltreated as children, but individuals with the same allele who were raised in supporting environments had a lower risk of antisocial behavior and ADHD than those with the more active version. A "short" allele in the serotonin transporter gene led to increased vulnerability to depression in response to stressful life events, but improved functioning versus those with the more typical "long" allele in the absence of stressful events.

6. Gillespie, C.F., Phifer, J., Bradley, B., & Ressler, K.J. (2009). "Risk and resilience: Genetic and environmental influences on development on the stress response." ***Depression and Anxiety, 26*****, 984-92.**

Polymorphisms within two key genes (*CRHR1* and *FKBP5*) affect lifetime risk of Post Traumatic Stress Disorder (PTSD) and depression in the face of childhood adversity. Specific *CRHR1* polymorphisms are associated with variations in antidepressant treatment response and suicide attempt history as a function of depression. Specific *FKBP5* polymorphisms, involved in

glucocorticoid receptor sensitivity regulation, significantly interacted with the severity of child abuse to predict the level of adult PTSD.

7. Krishnan, V., Han, M.H., Graham, D.L., Berton, O., Renthal, W., Russo, S.J., LaPlant, Q., … Nester, E.J. (2007). "Molecular adaptations underlying susceptibility and resistance to social defeat in brain reward regions." ***Cell, 131*****, 391-404.**

Mice Susceptible and Unsusceptible to social defeat were studied. Unsusceptible mice were immune to the increased depression and decreased in body weight observed in Susceptible mice. Unsusceptible mice had a larger number of gene regulations than Susceptible mice, suggesting the resistant phenotype is an active neurobiological process rather than simply an absence of vulnerability. Mice with a particular BDNF mutation (Met/Met) had an Unsusceptible phenotype and reduced levels of BDNF, suggesting that a naturally occurring impairment in activity-dependent BDNF release promotes resistance to social defeat.

8. Caspi, A., McClay, J., Moffitt, T.E., Mill, J., Martin, J., Craig, I.W., Taylor, A., …Poulton, R. (2002). "Role of genotype in the cycle of violence in maltreated children." ***Science 297*****, 851-4.**

A functional polymorphism in the gene encoding for monoamine oxidase A (MAOA) leading to high levels of MAOA expression led to reduced risk of antisocial behavior in the face of childhood maltreatment. The MAOA enzyme is responsible for metabolizing other neurotransmitters, and genetic deficiencies in MAOA are associated with increased aggression in mice and humans.

9. Zhou, Z., Zhu, G., Hariri, A., Enoch, M., Scott, D., Sinha, R., Virkkunen, M., … Goldman, D. (2008). "Genetic variation in human NPY expression affects stress response and emotion." ***Nature*****,** ***452*****, 997-1002.**

Haplotype-drive changes in expression of Neuropeptide Y, an anxiolytic released in response to stress, are associated with variation in brain response to emotional and stress challenges. Lower expression of NPY is associated with higher emotion-induced activation of amygdala and diminished resilience as assessed by pain/stress-induced activations of endogenous opioid neurotransmission in various brain regions.

10. Redei, E.E. (2008). "Molecular genetics of the stress-responsive adrenocortical axis." ***Annals of Medicine, 40*** **(2), 139-48.**

This article reviews the polygenetic contributions to individual variation in basal and stimulated plasma glucocorticoid levels. Animal studies reviewed illustrate that the stress-responsive adrenocortical function significantly depends on susceptible genotype.

11. Schjolden, J., & Winberg, S. (2007). "Genetically determined variation in stress responsiveness in rainbow trout: Behavior and neurobiology." ***Brain Behavior and Evolution, 70*** **(4), 227-38.**

This article suggests coping mechanisms (proactive versus reactive) and physiological responses to stress such as cortisol response are heritable. Fish that produced low cortisol in response to an acute stressor had higher brain serotonin turnover and were proactive copers. Similar findings were reported in rodents and, in both species, low cortisol producers were more likely to be dominant in fights, aggressive and competitively superior.

12. De Kloet, E.R., Joels, M., & Holsboer, F. (2005). "Stress and the brain: From adaptation to disease." ***Nature Reviews Neuroscience*****, *6*, 463-75.**

This article gives evidence that early adversity, in combination with genotype, seems to sensitize certain circuits in the brain such as the HPA axis to an acute stressor. Specifically, polymorphisms in a glucocorticoid receptor (GR) gene led to variations in response to antidepressant therapy, healthier metabolic profiles and better cognitive function compared to the general population. Other functional polymorphisms in the GR gene are associated with more body fat, less lean mass, hypersensitive insulin secretion and enhanced corticotropin response to a psychosocial stressor.

13. Weaver, I.C.G., Cervoni, N., Champagne, F.A., D'Alession, A.C., Sharma, S., Seckl, J.R., Dymov, S., … Meaney, M.J. (2004). "Epigenetic programming by maternal behavior." ***Nature Reviews Neuroscience, 7*** **(8), 847-54.**

Increased maternal attention by rat mothers led to epigenetic changes in glucocorticoid receptors in the hippocampus of offspring. Offspring affected by these epigenetic changes were less fearful and showed a more modest response of the HPA axis to stress. Thus, genetic changes occurring after birth can have long-lasting effects on stress response and behavior.

14. Derijk, R.H. (2009). "Single nucleotide polymorphisms related to HPA axis reactivity." ***Neuroimmunomodulation, 16*** **(5), 340-52.**

This article reviews gene variants in the $GABA_A$ receptor, the μ-opioid receptor, serotonin transporter, catechol-O-methyltransferase (COMT), monoamine oxidase-A (MAOA), α-2 adrenergic receptor, BDNF, angiotensin-converting enzyme, mineralocorticoid receptor and glucocorticoid receptor that effect the HPA axis. The involvement of several different genes on HPA axis responsiveness indicates the complexity of the system and the need for optimal regulation.

15. Caspi, A., Sugden, K., Moffitt, T.E., Taylor, A., Craig, I.W., Harrington, H., McClay, J., …Poulton, R. (2003). "Influence of life stress on depression: Moderation by a polymorphism in the 5-HTT gene." ***Science*****, *201*, 386-9.**

A functional polymorphism (short versus long allele) in the promoter region of the serotonin transporter gene is described and is the first genetic variant identified as an inherited ~~re~~silience factor." Individuals homozygous (s/s) or heterozygous (s/l) for the short allele exhibited more depressive symptoms, diagnosable depression and suicidality in relation to stressful life events than individuals homozygous for the long allele (l/l).

16. Holmes, A. (2008). "Genetic variation in cortico-amygdala serotonin function and risk for stress-related disease." ***Neuroscience & Biobehavioral Review*****, *32* (7): 1293-314.**

The serotonin system is crucial to the acute stress response and chronic stress adaptation, and genetic variation in a multitude of molecules involved in this system can affect development and function of key neural circuits between neuroanatomical elements involved in the behavioral stress response (dorsal raphe nucleus, medial prefrontal cortex, amygdala) resulting in alterations in behavioral, physiological and neuroendocrinological responses to stress. The serotonin system is plastic, and the author suggests stress-related pathology manifests only when the net effect of multiple gene variants causes system-level failure.

17. Hariri, A.R., Mattay, V.S., Tessitore, A., Kolachana, B., Fera, F., Goldman, D., Egan, M.F., …Weinberger, D.R. (2002). "Serotonin transporter genetic variation and the response of the human amygdala." ***Science, 297*** **(5580), 400-4.**

Carriers with one or two copies of the short allele of the serotonin transporter gene *SLC6A4* exhibit greater amygdala blood flow and functional activity on fMRI in response to fearful stimuli. Imaging of the same subjects performing working memory tasks revealed no significant group differences, indicating that the increased excitability was associated specifically with emotional response.

18. Pezawas, L., Meyer-Lindenberg, A., Drabant, E., Verchinski, B., Minoz, K., Loachana, B., Egan, M., & Weinberger, D.R. (2005). "5-HTTLPR polymorphism impacts human cingulated-amygdala interactions: A genetic susceptibility mechanism for depression." ***Nature Reviews Neuroscience, 8*** **(6), 828-34.**

A short allele polymorphism in the serotonin transport gene promoter region leads to reduced transcriptional efficiency, increased anxiety and elevated risk of depression in the context of environmental adversity. On neuroimaging, carriers of the short allele had reduced gray matter volume in limbic regions critical for processing negative emotion and reduced coupling of the perigenual cingulate-amygdala circuit. Thus, the short allele genotype affects the structure and wiring of a region of the limbic system crucial for depression and anxiety-related temperamental traits.

19. Heinz, A., Braus, D.F., Smolka, M.N., Wrase, J., Puls, I., Hermann, D., Klein, S., …Buchel, C. (2005). "Amygdala-prefrontal coupling depends on a genetic variation of the serotonin transporter." ***Nature Reviews Neuroscience, 8*** **(1), 20-21.**

Carriers of the short allele of the serotonin transporter gene *SLC6A4* exhibited increased activation of amygdala and greater coupling between amygdala and ventromedial prefrontal cortex on fMRI when exposed to aversive, but not pleasant, pictures. These findings are similar to those seen in major depression.

Key Researchers

Stress/Hormones:
Bruce McEwen (The Rockefellar University)

Robert Sapolsky (Stanford University)
James Herman (University of Cincinnati)

Resilience / Hardiness:
George Bonanno (Columbia University)
Paul Bartone (National Defense University, Washington DC)
Salvatore Maddi (University of California Irvine)

Genetics:
Avshalom Caspi (University of Wisconsin and King‘s College - London)
Michael Rutter (King‘s College London)
Ahmad Hariri (Clinical Brain Disorders Branch, NIH)
E. Ron de Kloet (Leiden Amsterdam Center for Drug Research and Leiden University Medical Center)
Andrew Holmes (National Institute on Alcoholism and Alcohol Abuse, Maryland)
Terrie E. Moffitt (University of Wisconsin and King‘s College – London)

Chapter 3

Emotion and Cognition

This section includes twenty six papers discussing neurological and physiological indices of emotion regulation and the effect of emotion on cognitive ability. Several papers discuss the role of the amygdala in processing emotional stimuli and explain many factors that differentiate whether amygdala activation will lead to conscious, cortical activation. The underpinnings of both automatic emotion regulation and cognitive appraisal and their relationship with cognitive performance are also discussed. In general, the following list is intended to provide an overview of adaptive neurological and physiological mechanisms, following emotion elicitation, which could lead to enhanced cognitive performance.

1. **Phillips, M. L., Ladouceur, C. D., & Drevets, W. C. (2008). A neural model of voluntary and automatic emotion regulation: Implications for understanding the pathophysiology and neurodevelopment of bipolar disorder. *Molecular Psychiatry, 13*, 833-857.**

This article describes a new neural model of emotion regulation that includes voluntary and automatic regulatory subprocesses. They highlight two major neural systems: (1) a feedforward pathway: a medial prefrontal cortical system, including the orbital frontal cortex, subgenual anterior cingulated gyrus (ACG), rostral ACG, hippocampus and parahippocampus, and dorsomedial prefrontal cortex, and (2) a feedback pathway: a lateral prefrontal cortical system, including dorsolateral prefrontal cortex and ventrolateral prefrontal cortex.

2. **Winkielman, P., Knutson, B., Paulus, M., & Trujillo, J. L. (2007). Affective influence on judgments and decisions: Moving towards core mechanisms. *Review of General Psychology, 11*(2), 179-192.**

This article reviews psychological accounts of affective influence on judgments and decisions and argues that these accounts can be enriched by insights from biopsychology. The authors show how biopsychological research helps (1) reveal the sources of values and feelings; (2) predict when affect will influence attentional, perceptual, memorial, and decision processes; and (3) identify precise mechanisms underlying the interaction between affective and cognitive systems. These biopsychological considerations generate interesting predictions about when affective stimuli should influence subsequent behavior and feeling.

3. **Gray, J. R. (2001). Emotional modulation of cognitive control: Approach-withdrawal states double-dissociate spatial from verbal two-back task performance. *Journal of Experimental Psychology: General, 130*(3), 436-452.**

The results of this study suggest that approach-withdrawal states can have selective influences on components of cognitive control, possibly on a hemispheric basis. They support and extend several frameworks for conceptualizing emotion-cognition interactions. Performance on psychometrically matched spatial and verbal two-back tasks was influenced oppositely by induced approach and withdrawal emotional states. The overall pattern was that an approach state tended to impair spatial performance and improve verbal, whereas a withdrawal state tended to improve spatial performance and impair verbal.

4. **Green, M. J., & Malhi, G. S. (2006). Neural mechanisms of the cognitive control of emotion. *Acta Neuropsychiatrica, 18*, 144-153.**

A growing body of research implicates an inhibitory role of PFC and cingulate brain regions that exert cognitive control upon subcortical and cortical emotion generation systems. Recent deployment of concurrent physiological indexes of emotional arousal in neuroimaging studies has enabled a more precise understanding of the cognitive control of both subjective and physical emotional responses by cortical regions, such that the cortex undergoes complex modulation by means of feedback loops that stem from peripheral nervous system activity. Green and Malhi explain that the propensity to engage in maladaptive cognitive strategies in response to negative emotional experiences may alter the recruitment of neural mechanisms that potentiate negative effect.

5. **Ochsner, K. N., & Gross, J. J. (2005). The cognitive control of emotion. *TRENDS in Cognitive Sciences, 9*(5), 242-249.**

This article discusses why specific control strategies recruit specific control systems and the extent to which different strategies modulate appraisal systems in different ways. In general, studies of cognitive change have shown consistently that emotional appraisal systems can be modulated by PFC, OFC and cingulate control systems activated either (1) by high-level expectations for beliefs about, and interpretations of, stimuli, or (2) by learning to associate new emotional responses with stimuli. These findings are strikingly similar to control dynamics observed for ‗cold' forms of control that involve prefrontal and cingulate systems.

6. **Appelhans, B. M., & Luecken, L. J. (2006). Heart rate variability as an index of regulated emotional responding. *Review of General Psychology, 10*, 229-240.**

Heart rate variability is emerging as an objective measure of individual differences in regulated emotional responding. This article discusses a comprehensive set of theoretical and empirical explanations for why heart rate variability provides information regarding one's ability to regulate emotions. Unlike other psychophysiological variables, heart rate variability provides information regarding both parasympathetic nervous system and sympathetic nervous system activity, thereby permitting inferences about both inhibitory and excitatory processes in emotion regulation.

7. **Williams, L. E., Bargh, J. A., Nocera, C. C., & Gray, J. R. (2009). The unconscious regulation of emotion: Nonconscious reappraisal goals modulate emotional reactivity. *Emotion, 9*(6), 847-854.**

This study revealed that nonconscious emotion regulation is not only more successful than conscious appraisal, but that individuals who do not typically utilize reappraisal processes benefit most from nonconscious emotion regulation. The authors explain this finding as conscious appraisals having too many constraints and that this process may actually interrupt the human's natural ability to self-regulate.

8. **Gray, J. R., Braver, T. S., & Raichle, M. E. (2002). Integration of emotion and cognition in the lateral prefrontal cortex. *PNAS, 99*(6), 4115-4120.**

This study revealed a highly specific result, which indicates that emotion and higher cognition can be truly integrated, i.e., at some point of processing, functional specialization is lost, and emotion and cognition conjointly and equally contribute to the control of thought and behavior. Other regions in lateral PFC showed hemispheric specialization for emotion and for stimuli separately, consistent with a hierarchical and hemisphere-based mechanism of integration.

9. deVries, M., Holland, R. W., & Witteman, C. L. M. (2008). In the winning mood: Affect in the Iowa gambling task. *Judgment and Decision Making, 3*, 42-50.

This article suggests that an individual's state functions as a moderator of the type of process that guides decision-making. Specifically, in a happy mood state, people probably rely more strongly on affective reactions toward different decision options, whereas in a sad mood state, people adopt a more careful, analytical decision-strategy.

10. Carver, C. S., & Scheier, M. F. (1990). Origins and functions of positive and negative affect: A control process view. *Psychological Review, 97*, 19-35.

This publication discusses human behavior as a hierarchical organization with multiple feedback loops. It is explained that emotion can serve as a simple system interrupter that calls for a reassessment of expectancies that relies heavily on memory. Where goal attainment is likely, positive emotions and task engagement will follow. When goal attainment is unlikely, disengagement and negative affect will result.

11. Gray, J. A. (1990). Brain systems that mediate both emotion and cognition. *Cognition & Emotion, 4*(3), 269-288.

Neurobiological research with animals strongly suggests that the brain systems which mediate emotion overlap with those that mediate cognition to such a degree that it is difficult, if not impossible, to maintain any clear distinction between them. Possible reasons for this overlap are discussed; and a model of brain systems that simultaneously subserve emotion and cognition is presented. The model postulates the existence of three fundamental systems of this kind in the mammalian brain: a behavioral approach system, a fight/flight system, and a behavioral inhibition system.

12. Lazarus, R. S. (1991). *Emotion and adaptation*. New York: Oxford University Press.

This work provides a complete theory of emotional processes, explaining how different emotions are elicited and expressed. The author's approach puts emotion in a central role as a complex, patterned, organic reaction to both daily events and long-term efforts on the part of the individual to survive, flourish, and achieve. In his view, emotions cannot be divorced from other biological, social or cognitive functions. As coping and adapting processes, they are seen as part of the ongoing effort to monitor changes, stimuli, and stresses arising from the environment.

13. Gray, J. R. (2004). Integration of emotion and cognitive control. *Current Directions in Psychological Science, 13*(2), 46-48.

In this article, Gray defines the concept of ~~"in~~integration" in the context of emotion and cognition. He then provides an explanation for how cognition and emotion should function together, focusing on a cognitively flexible framework where adaptations are driven by emotions. Empirical data is then presented that supports the idea that emotion may actually modulate cognitive control.

14. Schneider, T. R. (2008). Evaluations of stressful transactions: What's in an appraisal? *Stress and Health, 24*, 151-158.

In this article, Schneider explains the psychological, physiological, and behavioral correlates of the threat and challenge stress appraisal. In addition, the article provides validation for a Stress Appraisal Scale that has been shown to determine an individual's psychological, physiological, and behavioral outcome when faced with a stressful task. The article used a difficult math task as compared to a real-world task to induce stress. Negative and positive emotions were recorded.

15. Hong-Yu, Y., & Wen-Juan, L. (2006). Neuroendocrine responses and memory performance induced by negative emotion. *Chinese Mental Health Journal, 20*(7), 421-424.

This article identified a relationship between explicit memory performance and individual responses of the sympathetic-nerve-system (SNS) and hypothalamus-pituitary-adrenal (HPA) axis following the inducement of negative stimuli. Specifically, this study found that negative emotional stimuli significantly increased systolic blood pressure, heart rate, and diastolic blood pressure. In addition, compared with neutral controls, the performance of explicit memory after unpleasant pictures significantly increased.

16. Carver, C. S., & Scheier, M. F. (2002). Control processes and self-organization as complementary principles underlying behavior. *Personality and Social Psychology Review, 6*, 304-315.

This article addresses the convergence and complementarity between self-regulatory control-process models of behavior and dynamic systems models. The control-process view holds that people have a goal in mind and try to move toward it (or away from it), monitoring the extent to which a discrepancy remains between the goal and one's present state and taking steps to reduce the discrepancy (or enlarge it). Dynamic systems models tend to emphasize a bottom-up self-organization process, in which a coherence arises from among many simultaneous influences, moving the system toward attractors and away from repellers. The authors suggest that these differences in emphasis reflect two facets of a more complex reality involving both types of processes.

17. Bartolic, E. I., Basso, M. R., Schefft, B. K., Glauser, T., & Titanic-Schefft, M. (1999). Effects of experimentally-induced emotional states on frontal lobe cognitive task performance. *Neuropsychologia, 37*(6), 677-683.

This study examined whether cognitive outcomes associated with the left and right frontal lobes are differentially influenced by dysphoric and euphoric affect. In a completely between-

groups design, euphoria resulted in better verbal than figural fluency performance, and dysphoria yielded better figural than verbal fluency outcomes. These findings are consistent with electrophysiological data concerning frontal lobe activity during euphoric and dysphoric affect, and they underscore the notion that affective influences upon cognition are more complicated than previously thought.

18. Yun, R. J., Krystal, J. H., & Mathalon, D. H. (2010). Working memory overload: Fronto-limbic interactions and effects on subsequent working memory function. *Brain Imaging and Behavior.* Online publication date: 20-Feb-2010.

This study employed functional magnetic resonance imaging in conjunction with a parametric working memory task to characterize the behavioral and neural effects of cognitive overload on subsequent cognitive performance, with particular attention to cognitive-limbic interactions. Overloading the working memory system was associated with varying degrees of subsequent decline in performance accuracy and reduced activation of brain regions central to both task performance and suppression of negative affect. These findings suggest that vulnerability to overload effects in cognitive functioning may be mediated by reduced amygdala suppression and subsequent amygdala-prefrontal interaction.

19. Erk, S., Kleczar, A., & Walter, H. (2007). Valence-specific regulation effects in a working memory task with emotional context. *Neuroimage, 37*(2), 623-632.

This study tested the effects of emotional stimulation during active maintenance of information using the Sternberg item recognition task with two load conditions. Data revealed no impairment of working memory performance during emotional context. Performance was better for emotional compared to neutral context during high load. High cognitive effort was associated with reduced activity in emotion processing regions, i.e. the amygdala and ventral striatum. This effect was mediated by different prefrontal regions, i.e. by left inferior PFC for negative and left superior PFC for positive valence.

20. Ohman, A. (2005). The role of the amygdala in human fear: automatic detection of threat. *Psychoneuroendocrinology, 30*(10), 953-958.

This article discusses two different neural activation pathways following fear induction. When the stimulus conditions allow conscious processing, the amygdala response to feared stimuli is enhanced and a cortical network that includes the anterior cingulate cortex and the anterior insula is activated. However, the initial amygdala response to a fear-relevant but non-feared stimulus (e.g. pictures of spiders for a snake phobic) disappears with conscious processing and the cortical network is not recruited. Instead there is activation of the dorsolateral and orbitofrontal cortices that appears to inhibit the amygdala response.

21. Hairir, A. R., Mattay, V. S., Tessitore, A., Fera, F., & Weinberger, D. R. (2003). Neocortical modulation of the amygdala response to fearful stimuli. *Biological Psychiatry, 53*(6), 494-501.

In this study, blood oxygen level dependent functional magnetic resonance imaging revealed that whereas perceptual processing of International Affective Picture System stimuli was

associated with a bilateral amygdala response, cognitive evaluation of these same stimuli was associated with attenuation of this amygdala response and a correlated increase in response of the right prefrontal cortex and the anterior cingulate cortex. Moreover, this pattern was reflected in changes in skin conductance.

22. Lerner, J. S., Dahl, R. E., Hariri, A. R., & Taylor, S. E. (2007). Facial expressions of emotion reveal neuroendocrine and cardiovascular stress responses. *Biological Psychiatry, 61*, 253-260.

This article describes cardiac and neuroendocrine responses to negative emotional stimuli. The participants were categorized as responding to the negative stimuli with either a fear or indignation (anger and disgust) facial profile. The results reveal that individuals who exhibited fear responses also exhibit elevated cardiac and neuroendocrine reactivity. Individuals who exhibited indignation to the stimuli showed inhibited cardiac and neuroendocrine reactivity.

23. Mauss, I. B., Cook, C. L., Cheng, J. Y. J., & Gross, J. J. (2007). Individual differences in cognitive reappraisal: Experiential and physiological responses to an anger provocation. *International Journal of Psychophysiology, 66*, 116-124.

In the present study, we sought to address the question of whether individual differences in reappraisal are associated with an adaptive profile of responding to a laboratory anger provocation. Results indicated that compared to low reappraisers, high reappraisers had a more adaptive profile of emotion experience and cardiovascular responding. These findings suggest that reappraisers are successful at down-regulating negative emotions, even in the context of a potent negative emotion such as anger.

24. Ekman, P., Levenson, R. W., & Friesen, W. V. (1983). Autonomic nervous system activity distinguishes among emotions. *Science, 221*, 1208-1210.

This article is critical to understanding autonomic nervous system responses for various emotions. It describes differentiating cardiac reactivity for positive and negative emotions, while also further differentiating negative emotions. Specifically, heart rate increased for negative emotions, but decreased for positive emotions, while skin temperature only increased for anger.

25. Rohrbaugh, J. W., Sirevaag, E. J., Stern, J. A., & Ryan, A. H. (2006). The physiology of threat: Remote assessment using laser Doppler vibrometry. *The Journal of Credibility Assessment and Witness Psychology, 7*(2), 135-145.

This article introduces a noninvasive technique (laser Doppler vibrometry) for identifying changes in physiological activity due to emotional responses. The article is framed for a witness credibility assessment, which applies to enemy interrogation. Laser Doppler Vibrometry (LDV) provides advanced measures in multiple physiological systems relevant to laboratory and field assessment of stress and emotion, including cardiovascular reactivity, tremor, and muscle vibration.

26. Dalgleish, T. (2004). The emotional brain. *Nature Reviews Neuroscience, 5*, 582-589.

This article lays out a comprehensive timeline of affective neuroscience. It describes many viewpoints and theories as well as graphic representations of critical areas of the human brain. In addition, the article discusses the future of affective neuroscience with particular emphasis on new technologies and methods, such as functional imaging and transcranial magnetic stimulation (TMS).

Key Researchers

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Chapter 4

Vigilance

This section contains 26 papers describing the use of neuroergonomic procedures in the study of sustained attention. Vigilance or sustained attention tasks require observers to maintain their focus of attention and to detect transient and infrequent signals over prolonged periods of time. The ubiquitous fining in vigilance research is that performance declines over time, this is known as the vigilance decrement. The role of workers have transformed from that of active controllers to system executive who monitor the functioning of machines that do the work for them and intervene only in the event of potentials problems. Being that many accidents have been attributed to the vigilance failures of human operators, an understanding of the factors that influence vigilance performance and their underlying mechanisms are crucial for system integrity and public safety. This section reviews the relevant literature in the investigation of tools used to measure the hemodynamics of the brain as it relates to vigilance performance.

1. **Berka, C., Levendowski, D. J., Lumicao, M. N., Yau, A., Davis, G., Zivkovic, V. T., Olmstead, R. E., …Craven, P.L. (2007). EEG correlates of task engagement and mental workload in vigilance, learning, and memory tasks. *Aviation, Space, and Environmental Medicine, 78 (Suppl. 1),* B231-B244.**

This article explored the capability of electroencephalographic to monitory levels of task engagement and mental workload for a variety of cognitive tasks. The authors found that EEG workload increases with increasing working memory load and during problem solving, integration of information, analytical reasoning, and may be more reflective of executive functions. They found that EEG measures correlated with subjective and objective performance metrics.

2. **Butti, M., Contini, D., Molteni, E., Caffini, M., Spinelli, L., Baselli, G., Bianchi, A. M., …Torricelli, A. (2009). Effect of prolonged stimulation on cerebral hemodynamic: a time resolved fNIRS study. *Medical Physics, 36,* 4103-4114.**

In this article, the authors address the topic of characterizing the dynamics of cerebral metabolism in the prefrontal cortex during a continuous performance task by means of functional near-infrared spectroscopy. Oxygenated hemoglobin showed a steady decrease over time then a rapid increase immediately following the task.

3. **Coull, J. T., Frith, C. D., Frackowiak, R. S., & Grasby, P. M. (1996). A fronto-parietal network for rapid visual information processing: a PET study of sustained attention and working memory. *Neuropsychologia, 34,* 1085-1095.**

This study investigated the functional anatomy of the rapid visual information-processing task using positron emission tomography derived measures of regional cerebral blood flow. The task increased rCBF bilaterally in the inferior frontal gyri, parietal cortex and fusiform gyrus, and in the right frontal superior gyrus rostrally. Data are consistent with the existence of a right fronto-parietal network for sustained, and possibly selective, attention, and a left fronto-parietal network for the phonological loop component of working memory.

4. **Fallgatter, A. J. & Strik, W. K. (1997). Right frontal activation during the continuous performance test assessed with near-infrared spectroscopy in healthy subjects. *Neuroscience Letters, 223,* 89-92.**

In the present study, two-channel NIRS was utilized to investigate brain oxygenation. Significant differences between the left and right hemisphere were found in deoxyhaemoglobin, but not in oxyhaemoglobin in right frontal brain areas as compared to baseline during the test. The findings suggest that the sensitivity of the NIRS-method is sufficient to detect brain oxygenation changes during cognitive activation.

5. **Funke, M. E., Warm, J. S., Matthews, G., Finomore, V., Vidulich, M. A., Knott, B. A., Helton, W. S., … Parasuraman, R. (2010). Static and dynamic discriminations for vigilance: effects on cerebral hemodynamics and workload. In T. Marek, W. Karwowski, & V. Rice (Eds.), Advances in Understanding Human Performance: Neuroergonomics, Human Factors Design, and Special Populations. Boca Raton, Florida: Taylor and Francis.**

This study investigated the belief that responses such as measurements of accuracy and speed to a vigilance task are interchangeable indices of the same underlying processes. Data presented in this study indicate that there are major differences between these types of tasks in terms of cerebral hemodynamics as measured by transcranial Doppler sonography and perceived mental workload. They found that there was a right hemispheric dominance for the dynamic task, requiring measurement of accuracy, as well as a significant decrease in CBF over time. These measures were also accompanied by greater perceived mental workload ratings.

6. **Helton, W. S., Hayrynen, L., & Schaeffer, D. (2009). Sustained attention to local and global target features is different: performance and tympanic membrane temperature. *Brain and Cognition, 71,* 9-13.**

In this experiment, participants performed a sustained attention task requiring either global or local letter target discriminations. Tympanic membrane temperature (TMT) was utilized in this study as an index of cerebral activation. Participants in the global letter detection condition had slower reaction times as well as elevated post-task right TMT indicative of reduced cerebral activation in the right hemisphere, in comparison to participants in the local letter detection or no-work imperative conditions. Both the performance and physiological results of this study indicate increased cognitive fatigue when global feature discriminations are required.

7. **Helton, W. S., Hollander, T. D., Warm, J. S., Tripp, L. D., Parsons, K., Matthews, G., Dember, W. N., …Hancock, P.A. (2007). The abbreviated vigilance task and cerebral hemodynamics. *Journal of Clinical and Experimental Psychology, 29,* 545-552.**

Transcranial Doppler sonography and near-infrared spectroscopy measures of cerebral blood flow velocity and oxygenation levels were collected during an abbreviated 12-min vigilance task. Both the TCD and NIRS measures showed higher levels of cerebral vascular activity in the right

than in the left cerebral hemisphere. There was a significant decline in performance over time however no significant change in the physiological measures over time.

8. **Helton, W. S., Kern, R. P., & Walker, D. R. (2009). Tympanic membrane temperature, exposure to emotional stimuli and the sustained attention to response task. *Journal of Clinical and Experimental Neuropsychology, 31,* 611-616.**

This study investigated lateral differences in tympanic membrane temperature. Right TMT changed significantly more from baseline TMT than did left TMT after participants performed SARTs, a finding consistent with previous research indicating right cerebral dominance for sustained attention and response inhibition. Overall, these results support TMT as a useful and very cost effective index of cerebral lateralization.

9. **Helton, W. S., Warm, J. S., Tripp, L. D., Matthews, G., Parasuraman, R., & Hancock, P. A. (2010). Cerebral lateralization of vigilance: a function of task difficulty. *Neuropsychologia, 6,* 1683-1688.**

Functional near infrared spectroscopy measures of cerebral oxygenation levels were collected from participants performing difficult and easy versions of a 12min vigilance task. The fNIRS measurements in both vigilance tasks showed higher levels of cerebral activity than was present in the case of the no-work controls. In the easier task, greater activation was found in the right than in the left cerebral hemisphere, matching previous results indicating right hemisphere dominance for vigilance. However, for the more difficult task, this laterality difference was not found, instead activation was bilateral.

10. **Hitchcock, E. M., Warm, J. S., Matthews, G., Dember, W. N., Shear, P. K., Tripp, L. D., Mayleben, D. W., …Parasuraman, R. (2003). Automation cueing modulates cerebral blood flow and vigilance in a simulated air traffic control task. *Theoretical Issues in Ergonomics Science, 4,* 89-112.**

This study utilized transcranial Doppler sonography to examine the influence of automation cues of varying reliability on vigilance performance. The demonstration of systematic modulation of cerebral blood flow with time on task, automation cueing and signal salience provides strong evidence for a right hemispheric brain system that is involved in the functional control of vigilance performance.

11. **Kirmizi-Alsan, E., Bayraktaroglu, Z., Gurvit, H., Keskin, Y.H., Emre, M., & Demiralp, T. (2006). Comparative analysis of event-related potentials during Go/NoGo and CPT: Decomposition of electrophysiological markers of response inhibition and sustained attention. *Brain Research, 1104,* 114-128.**

This study set out to decompose the components of two frontal executive function tests, Go/NoGo and cued continuous performance task, by analyzing event-related potentials. Results suggest that theta component reflects response inhibition in both GNG and CPT, whereas delta component reflects the more demanding sustained attention requirement of the CPT. The latency

prolongation observed with the NoGo condition of the CPT paradigm was thought to be due to perseverance/inhibition conflict enhanced by the primer stimuli in CPT.

12. Lavine, R.A., Sibert, J.L., Goktuek, M., & Dickens, B. (2002). Eye-tracked measures and human performance in a vigilance task. *Aviation, Space, and Environmental Medicine, 73,* 367-372.

This study investigated eye-tracking measures on a visual vigilance task. They found that dwell time, number, and accuracy of fixation on target objects decreased with time on task, and inaccurate scan-paths were often associated with increase in performance errors and subjective ratings of fatigue.

13. Lawrence, N. S., Ross, T. J., Hoffmann, R., Garavan, H., & Stein, E. A. (2003). Multiple neuronal networks mediate sustained attention. *Journal of Cognitive Neuroscience, 15,* 1028-1038.

Functional MRI was used to investigate the neural substrates of sustained attention in order to better understand the neural networks underlying attentional abilities. Brain regions where task-induced activation correlated with task performance were identified. Good task performance, as defined by better detection of target stimuli, was correlated with enhanced activation in predominantly right fronto-parietal regions and with decreased activation in predominantly left temporo-limbic and cingulate areas. Factor analysis revealed that these performance-correlated regions were grouped into two separate networks comprised of positively activated and negatively activated intercorrelated regions.

14. Matthews, G., Warm, J. S., Reinerman-Jones, L. E., Langheim, L. K., Washburn, D. A., & Tripp, L. (2010). Task engagement, cerebral blood flow velocity, and diagnostic monitoring for sustained attention. *Journal of Experimental Psychology, in press.*

This article investigated whether scores on a diagnostic battery would predict subsequent sustained attention. Subjective (Dundee Stress State Questionnaire & Coping in Task Situations Questionnaire) and psychophysiological (cerebral bloodflow velocity as measures by Transcranial Doppler sonography) indexes were measured during the battery and after the sensory or cognitive vigilance task. Task engagement, task focused coping, and CBFV to the battery were positively correlated, suggesting that they may index a common biocognitive energization response. They all predicted performance on both vigilance tasks thus potentially being a useful tool for diagnostic monitoring in applied settings.

15. O'Connell, R. G., Dockree, P. M., Robertson, I. H., Bellgrove, M. A., Foxe, J. J., & Kelly, S. P. (2009). Uncovering the neural signature of lapsing attention: electrophysiological signals predict errors up to 20 s before they occur. *The Journal of Neuroscience, 29,* 8604-8611.

The present study examined the temporal dynamics of electrocortical signals preceding a lapse of sustained attention. They found that activity increased in the αband (8–14 Hz)

beginning ~20sec before a missed target. Results show that the specific neural signatures of attentional lapses are registered in the EEG up to 20 sec before an error.

16. Parasuraman, R., Warm, J.S., & See, J.E. (1998). Brain systems of vigilance. In R. Parasuraman (Ed.), *The attentive brain* (221-256). Cambridge, MA: MIT Press.

This chapter reviews the research pertaining to the relationship between human vigilance and brain systems that regulate cortical arousal and the brain structures and networks associated with vigilance decrement. The evidence indicates that vigilance is related to but also distinct from cortical arousal and unified arousal theory.

17. Parasuraman, R. (1984). The psychobiology of sustained attention. In J.S. Warm (Ed.), *Sustained attention in human performance* (pp. 61-101). London: Wiley.

This chapter reviews the different neuro systems that are associated with each aspect of vigilance performance (overall level of vigilance, vigilance decrement as related to response criterion as well as in the decrements in perceptual sensitivity in the task).

18. Parasuraman, R. (2009). Assaying individual differences in cognition with molecular genetics: theory and application. *Theoretical Issues in Ergonomics Science, 10,* 399-416.

This paper outlines a theoretical framework for assessing individual differences in human performance by identifying normal variations in neurotransmitter genes linked to brain networks involved in specialized cognitive functions. Variants of genes can be associated with individual differences in basic cognitive functions such as selective attention, working memory, and vigilance.

19. Paus, T., Zatorre, R. J., Hofle, N., Caramanos, J. G., Petrides, M., & Evans, A. C. (1997). Time related changes in neural systems underlying attention and arousal during the performance on an auditory vigilance task. *Journal of Cognitive Neuroscience, 9,* 392-408.

Cerebral blood flow as measured by positron emission tomography and electroencephalographic activity were obtained from an auditory vigilance task. The study found that reaction time and EEG activity in the theta (4 to 7 Hz) range progressively increased across testing. CBF in several subcortical structures and cortical areas decreased as a function of time-on-task and there changes were limited to the right hemisphere. The authors suggest that the observed time-related changes in reaction time, EEG activity, and blood flow in the temporalis muscles are related to changes in the level of alertness and that CBF changes in the thalamus-related neural circuitry represent a brain correlate of such changes.

20. Schnittger, C., Johannes, S., Arnavaz, A, & Münte, M. F. (1997). Relation of cerebral blood flow velocity and level of vigilance in humans. *Neuroreport, 8,* 1637-1639.

Blood flow velocities in both middle cerebral arteries were measured using transcranial Doppler sonagraphy in participants engaged in a visual vigilance task. Performance changes

were paralleled by a decrease in CBFV in both MCAs. No hemispheric differences were seen. These data suggest a close coupling of performance and blood flow in vigilance tasks. Modulation of cholinergic activity during the vigilance task might be the common underlying mechanism.

21. Schultz, N. B., Matthews, G., Warm, J. S., & Washburn, D. A. (2009). A transcranial Doppler sonography study of shoot/don't-shoot responding. *Behavior Research Methods, 41,* 593-597.

This study examined the relationship between changes in cerebral blood-flow velocity, measured by transcranial Doppler sonography, and performance on a speeded shoot/don't-shoot task. They found decrease in both the performance measures and hemovelocity. Hemovelocity slowed across the left and right hemispheres as the task progressed, and hemovelocity was slower in the right hemisphere than in the left hemisphere.

22. Shaw, T. H., Warm, J. S., Finomore, V., Tripp, L., Matthews, G., Weiler, E., & Parasuraman, R. (2009). Effects of sensory modality on cerebral blood flow velocity during vigilance. *Neuroscience Letters, 461,* 207-211.

Transcranial Doppler sonography was used to measure cerebral blood flow velocity during the performance of an auditory and visual vigilance tasks. Signal detection responses and CBFV declined significantly over time in a linear manner for both modalities. In addition, the overall level of CBFV and the temporal decline in this measure were greater in the right than the left cerebral hemisphere. The results are consistent with the view that a right hemispheric system is involved in the functional control of vigilance and that this system operates in a similar manner in the auditory and visual channels.

23. Warm, J. S. & Parasuraman, R. (2007). Cerebral hemodynamics and Vigilance. In R. Parasuraman & M. Rizzo (Eds.), *Neuroergonomics: The brain at work* (146-158). New York: Oxford University Press.

This chapter reviews a series of studies that explored the relationship between vigilance performance and cerebral hemodynamics with use of transcranial Doppler sonography and near-infrared spectroscopy. These studies have revealed a close coupling between vigilance performance and CBFV. This paper demonstrates the systematic modulation of blood flow velocity in the right cerebral hemisphere with time on task, memory load, signal salience, cueing, and the detection of feature absence or presence all provides evidence for a right hemispheric brain system that is involved in the functional control of vigilance performance over time.

24. Warm, J. S., Matthews, G., Parasuraman, R. (2009). Cerebral hemodynamics and vigilance performance. *Military Psychology, 21:(Suppl.1),* S75-S100.

Five studies are described using transcranial Doppler sonography and near-infrared spectroscopy to examine brain systems in vigilance. The results indicate that the vigilance decrement is paralleled by a decline in CBFV as indexed by TCD. In addition, both measures

showed greater activity in the right than in the left cerebral hemisphere in response to a variety of psychophysical challenges, indicating a right hemispheric system in control of vigilance performance. The TCD measure was also found to be potentially useful in selecting observers for vigilance assignments.

25. Warm, J. S., Parasuraman, R., & Matthews, G. (2008). Vigilance requires hard mental work and is stressful. *Human Factors, 50,* 433-441.

This paper reviews and summaries the current theoretical views of sustained attention research. The authors describes data to support that vigilance tasks require hard mental work and are stressful rather than what once was thought as understimulating and benign tasks. Neuroimaging studies using Transcranial Doppler sonography provides strong, independent evidence for resource changes linked to performance decrements in vigilance tasks.

26. Wingen, M., Kuypers, K. P. C., van de Ven, V., Formisano, E., & Ramaekers, J. G. (2008). Sustained attention and serotonin: a pharmaco-fMRI study. *Human Psychopharmacology: Clinical and Experimental, 23,* 221-230.

The present study assessed the influence of increased serotonin levels on brain areas involved in sustained attention. Although there were no differences in the vigilance performance between the control and serotonin groups functional magnetic resonance imaging showed less activation in the caudate nucleus, thalamus, and frontal areas and subjective measures found that the serotonin group has decrease alertness.

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Chapter 5

Trust

Research involving the neurophysiological assessment of trust is new and expanding area, paralleling the expansion of trust research generally in recent years. To date, there has been relatively little work in this area; much has been focused on revealing the mechanisms and brain areas associated with trust and mistrust. The amygdala has received considerable focus due to demonstrated involvement with processing fearful stimuli; the anterior cingulate has also been implicated due to the need for conflict resolution. Several major studies have concluded that the neuropeptide oxytocin plays a significant role in mediating trusting behavior, in part by influencing the amygdala. Much remains unknown about the process of forming and maintaining trust, or about the differences between human-human and human-machine trust.

1. **Adolphs, R., Tranel, D., & Damasio, A.R. (1998). The human amygdala in social judgment. *Nature*, 393,470-474.**

Adolphs, Tranel and Damsio (1998) found that individuals with bilateral amygdala damage rated the faces of untrustworthy and unapproachable individuals (as rated by controls) as approachable and trustworthy. However, they found that this effect did not extend to verbal descriptions (adjectives of personality attributes) of individuals. Thus, the researchers concluded that the amygdala, which has a role in processing threatening stimuli, may have a more specific role in triggering emotionally relevant information in response to visual stimuli (in this case, faces) that are potentially dangerous.

2. **Baumgartner, T., Heinrichs, M., Vonlanthen, A., Fishbacher, U., & Fehr, E. (2008). Oxytocin shapes the neural circuitry of trust and trust adaptations in humans. *Neuron*, 58, 639-650.**

Participants in this study played a monetary trust game with either a human or computer partner, after receiving oxytocin or a placebo. Despite violations of trust, the oxytocin group continued to invest with human partners, while the placebo group did not. fMRI testing revealed that during human partner trials, the oxytocin group had significantly less activation in the amygdala and midbrain, which are areas involved in fear processing, than those in the placebo group. These participants also had less activation in the caudate nucleus, which is an area that uses feedback to help individuals learn cause and effect relationships. There were no such differences in trials with the computer partner.

3. **Caldu, X., & Dreher, J.C. (2007). Hormonal and genetic influences on processing reward and social information. Annals of New York Academy of Sciences, 1118, 43-73.**

This extensive review article shows how reward processing and social interaction processes (including trust) share common neural substrates and how individuals‘ hormones and genes both affect these processes. Numerous brain areas, hormones, and genetic markers have been demonstrated to influence social interaction.

4. **Delgado, M., Rank, R. & Phelps, E. (2005). Perceptions of moral character modulate the neural systems of reward during the trust game. *Nature Neuroscience*, 8, 1611-1618**.

This study investigated the influence of social learning on choice. They found that individuals who believed that they were playing the Trust Game with morally good or morally bad partners (as compared to neutral partners), continued to make choices based on that knowledge, instead of updating their evaluations as they normally would. Interestingly, the researchers found that differential activation in the caudate nucleus, which would normally occur between positive and negative outcomes of the game, were diminished in the trials where the participant had information about their partner‘s good or bad moral standing.

5. **Fehr, E. (2008). The effect of neuropeptides on human trust and altruism: A neuroeconomic perspective. In D. Pfaff, C. Kordon, P. Chanson & Y. Christen (eds.) *Hormones and Social Behaviour* (pp.47-56). Berlin: Springer**.

The intranasal administration of oxytocin does not make investors more optimistic about trustees‘ generosity, nor does it make trustees more generous, and it only affects investors in social situations. However, oxytocin does make investors likely to invest more of their money with trustees, and it makes them less likely to change their investment strategy, even when they learn that their partners have defected on half of the trials. It is hypothesized that oxytocin creates these results by reducing the activation in the amygdala, which processes fearful stimuli. As a result, it helps participants overcome their betrayal aversion (in this case, to their detriment).

6. **Kosfeld, M., Heinrichs, M., Zak, P.J., Rischbacher, U., & Fehr, E. (2005). Oxytocin increases trust in humans. N*ature*, 435, 673-676.**

In this study, participants played one cycle of the Trust Game. Half of the participants in the investor role (Subject 1) were given a dose of intranasal oxytocin, and the other half (control group) were given a placebo. Those given the oxytocin trusted their partners with 17% larger transfers than those in the control group. Additionally, 45% of the participants in the oxytocin group invested all of their money, showing maximal trust, as compared to 21% in the control group. However, when the trustees were dosed with oxytocin, there were no significant changes to the amount of money returned to the investors. This could be because investors and trustees are facing essentially different situations. A second study concluded that oxytocin does not increase risk-taking behavior. Finally, additional analysis revealed that the oxytocin group and the control group were equally optimistic about the outcome.

7. **Krueger, F., McCabe, K., Moll, J., Kriegeskorte, N., Zahn, R., Strenziok, M., Heinecke, A., & Grafman, J. (2007). Neural correlates of trust. *Proceedings of the National Academy of Sciences of the United States of America*, 104(50), 20084-20089.**

This study used a reciprocal Trust Game and hyperfunctional magnetic resonance imaging (hyperfMRI) to explore the brain regions that are activated when people employ conditional and unconditional trust strategies. They found that the participants who never defected on their partners (unconditional trust) showed more activation in the paracingulate cortex (PcC) early in the game (during the trust building stage) than in the later stage (trust maintenance stage) like the defector group (who were only able to foster conditional trust). This early activation of the PcC helped the non-defector group build mental models of their partners' intentions and allowed them to form social attachments to each other in the maintenance stage, which was evidenced by activation in the septal area (SA). During the maintenance stage, the non-defector group also showed less activity in the ventral tegmental area (VTA) than the defector group, which meant that they were not working to understand which behaviors led to rewards like the defector group was forced to do (because they were still working to form mental models of their partners).

8. Krueger, F., Grafman, J., & McCabe, K. (2008). Neural correlates of economic game playing. *Philosophical Transactions of the Royal Society: Biological Sciences*, 363, 3859-3874.

This article reviewed research on economic game playing, which included studies that used games like: the Ultimatum game, the Equal Split Game, the Dictator Game, the Trust Game and Investment Game. Studies have found that more noradrenalin in participants' systems seem to make them play more cooperatively; the same is true of more serotonin in participants' systems. The opposite is true when participants are L-tryptophan depleted. However, participants are able to overcome the L-tryptophan deficiency by the second day of play and begin playing cooperatively again. For second players, unfair offers cause activation in the bilateral anterior insula (AI) and the anterior cingulated cortex (ACC) and the bilateral dorsolateral prefrontal cortex (DLPFC). Authors believe that the activation in the anterior insula reflects the participant's level of emotional resentment, and they have found that the higher the level of activation, the greater the chance is that the participant will reject the offer. Additionally, the authors believe that the ACC activation is due to the conflict that arises between their own self interest and the unfairness of the offer. Finally, the DLPFC activation, according to their theory, occurs when the participant tries to control the impulse to reject the unfair offer.

9. Rilling, J.K., Sanfey, A.G., Aronson, J.A., Nystrom, L.E., & Cohen, J.D. (2004). Opposing BOLD responses to reciprocated and unreciprocated altruism in putative reward pathways. *Neuroreport*, 15(16) 2539-2243.

In this study, participants played single-shot trials of the Prisoner's Dilemma game with study confederates, and with a computer; they also participated in a control task where they could choose between either: $0 and $5 or between $0 and $0. The researchers, using fMRI, explored the possibility that the firing frequency of midbrain dopamine neurons would be increased by reciprocated cooperation and decreased by unreciprocated cooperation. Indeed, they found this was true in their areas of interest, ventral striatum and the ventromedial prefrontal cortex, but only when the participants dealt with humans. Other patterns of activation were observed while playing with the computer and during the control task. This result suggests that, through the feedback provided by the dopamine system, humans may learn to distinguish between those who can and cannot be trusted.

10. Zak, P.J. (June, 2008). The neurobiology of trust. *Scientific American*, 298-88-95.

This study used one cycle of the Trust Game (Subject 1 was given $10). The researchers drew blood immediately after the Subject 2s decided how much money to return to Subject 1s. Subject 2s who were trusted by the Subject 1s saw a boost in their oxytocin levels afterward - it feels good when someone trusts you, and this recognition motivates you to reciprocate. The researchers concluded that the release of oxytocin acted as a signal to people that their ‗partner' could be trusted.

11. Porges, S. (1995). Orienting in a defensive world: Mammalian modifications of our evolutionary heritage. A polyvagal theory. Psychophysiology, 32, 301-318.

The polyvagal theory provides an evolutionary perspective of the autonomic nervous system. It proposes that mammals' current autonomic nervous system is made up of three systems. The phylogenetically oldest system is the unmyelinated visceral vagus (or vegetative vagus), which responds to threatening situations with immobilization; this is a residual strategy that is effective in reptiles, but can actually be lethal to mammals. Of the three systems, this is usually the last to be employed. The second strategy is one where the sympathetic nervous system increases metabolic output in order to prepare for fight or flight; this strategy is usually employed second. The last system, which is phylogenetically the most recent, is the myelinated vagus. The myelinated vagus originates in the nucleus ambiguus and ‗contains special visceral efferents that innervate the somatic musculature of the soft palate, larynx, pharynx, and esophagus' (309). Along with the vagal brake on the heart, this system provides the motor pathways for communication and emotion and fosters socialization.

12. Porges, S. (2001). The polyvagal theory: phylogenetic substrates of a social nervous system. International Journal of Psychophysiology, 42, 123-146.

This paper, as compared to the Porges's 1994 paper, focuses more on the vagus's role in social behavior. The author posits that the myelinated vagal system, which provides neural control of the heart, allows mammals to engage in potentially dangerous situations (like socializing with others who are not a part their familial group), because they are able to rapidly withdraw from the situation if needed without incurring the high biological cost that comes from relying on sympathetic-adrenal activation (like fish and reptiles must do) for withdrawing.

13. Porges, S. (2007). The Polyvagal perspective. *Biological Psychology*, 74(2), 116-143.

This article uses the principles of the Polyvagal Theory to demonstrate that the phylogeny of autonomic nervous system impacts human physiology in ways that have been overlooked by some traditional psychology and physiological research. As a result of these researchers' imperfect understanding of the autonomic nervous system, myths and inaccurate conclusions have been created. For instance, the author believes that cardiac vagal tone is not very useful in ‗understanding response strategies to environmental and visceral stimuli. Measures of more

specific vagal regulation, via either the nucleus ambiguus or the dorsal motor nucleus may provide more meaningful information‘ (p35). Porges concludes that it is necessary to _not only understand the vagal efferent actions on the heart from a neurophysiological level of inquiry, but the adaptive function of neural regulation of the heart must be interpreted within the context of the phylogeny of the autonomic nervous system‘ (34) for researchers to avoid making inaccurate conclusions in the future.

In this article, Porges also expands on his theory about myelinated vagal tone and its effect on social development. He notes that _the amplitude of respiratory sinus arrhythmia can be quantified to provide a sensitive index of the impact of the myelinated vagus on the heart‘ (p10). This method has been used in recent research, and several studies have found that children with stable RSA suppression have better social skills, fewer behavioral problems, and less negative emotional arousal in response to stressors.

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Chapter 6

Non-Invasive Brain Stimulation

This section contains forty-six journal articles which investigate various aspects of Non-Invasive Brain Stimulation. These papers include relevant information regarding the distinct methods used for brain stimulation, the positive and negative effects of brain stimulation on its subjects, and cognitive enhancements through brain stimulation.

1. Wasserman, E. M. (1997). Risk and safety of repetitive transcranial magnetic stimulation. *Electroencephalography and Clinical Neurophysiology*, *108*, 1-16.

This paper compares TMS to TDCS. TDCS has very mild side effects when compared to those produced by TMS. Larger electrodes allow for lower current density, and therefore produce very little, or no sensation. TDCS is not focal enough to map cortical functions within a centimeter, but evidence suggests that recorded effects are a result of the stimulus. TDCS cannot produce temporally focused effects on brain activity, such as momentary disruption of processing that makes TMS valuable for investigating cognition. TDCS's higher safety, lower cost, and ease of use make it a good alternative to TMS. DC polarization can change the efficiency of cognitive processes without side effects. TDCS can alter verbal fluency, motor learning, and perceptual thresholds and can be used with TMS simultaneously. DC polarization affects perceptual processes in a polarity-dependent way. Polarization of the visual cortex alters the amplitude of visual-evoked potentials, threshold for perception of TMS-induced phosphenes, and motion perception. Polarization of the parietal area has an analogous effect on tactile perception.

2. Wasserman, E. M., & Grafman, J. (2005). Recharging cognition with dc brain polarization. *TRENDS in Cognitive Science*, *9*(11), 503-505.

The article discusses risk and safety of rTMS and safety parameters of stimulation. rTMS may be useful for suppressing the development or spread of epileptogenic activity. rTMS stimulation of the prefrontal cortex affected mood. rTMS does have a tendency to produce seizures in normal patients if not following the written safety protocol. There are no long term adverse effects of rTMS shown by several neurophysiological tests. There is a significant decrease in the scores in memory tests 1 hour after stimulation. rTMS sometimes causes crying when left prefrontal area stimulated. Speech arrest followed by laughter was also observed. No hormone level changes result from rTMS except for in the patient who had a seizure. Hearing threshold permanently increased in animals after a single TMS pulse. rTMS may play a role in migraine relief.

3. Wagner, T., Valero-Cabre, A., & Pascual-Leone, A. (2007). Noninvasive human brain stimulation. *Annual Review of Biomedical Engineering*, *9*(19), 1-39.

The article discusses imaging technologies which are being used along with TMS and tDCS to better understand the effects of the stimulation. New imaging technologies such as DSI and MEG are also being considered.

4. **Massimini, M., Ferrarelli, F., Esser, S. K., Riedner, B. A., Huber, R., Murphy, M., Peterson M.J., & Tononi, G. (2007). Triggering sleep slow waves by transcranial magnetic stimulation. *The National Academy of Sciences of the USA*, *104*(20), 8496-8501.**

The article shows that rTMS can trigger slow wave sleep waves. After determining proper stimulation location and parameters, each TMS pulse reliably triggered a single slow wave with the same characteristics as original sleep wave. EEG returned to background level when TMS pulses ceased. TMS evoked slow oscillations (SOs) which were very similar in shape to normal SOs. TMS SOs originate in the same area under the coil whereas the natural SOs originate in several different places.

5. **Floel, A., & Cohen, L.G. (2006). Contribution of noninvasive cortical stimulation to the study of memory functions. *Brain Research Reviews*, *53*, 250-259.**

This article shows that low frequency TMS leads to depression of cortical excitability and high frequency rTMS leads to facilitation. Neural substrates of successful memory functions change over time. These changes are likely to play a compensatory role when elder individuals perform episodic memory tasks. TMS and tDCS are capable of enhancing or decreasing plasticity in the cerebral cortex. Methods to obtain long lasting effects are still being tested.

6. **Schutter, D. J.L.G., & Honk, J. (2005). Increased positive emotional memory after repetitive transcranial magnetic stimulation over the orbitofrontal cortex. *Journal of Psychiatry and Neuroscience*, *31*(2), 101-104**

The article shows that inhibitory rTMS over the left OFC as compared with placebo rTMS results in improved memory performance for happy faces. Functional neuroimaging studies have shown elevated OFC activity in depressed moods. This suggests that the left OFC may be an alternative brain region for TMS treatment of depression.

7. **Allen, E.A., Pasley, B.N., Duong, T., & Freeman, R.D. (2007). Transcranial magnetic stimulation elicits coupled neural and hemodynamic consequences. *American Association for the Advancement of Science*, *317*(10), 1918-1921.**

The article provides evidence that there is a long duration of neural and hemodynamic changes from a short application of TMS. TMS has the ability to disrupt precise timing of signals between interconnected neurons. This advocates its ability to alter brain plasticity. Hemodynamic and neural changes are long lasting and co-vary with stimulation duration and frequency.

8. **Harmer, C.J., Thilo, K.V., Rothwell, J.C., & Goodwin, G.M. (2001). Transcranial magnetic stimulation of medial-frontal cortex impairs the processing of angry facial expressions. *Nature Publishing Group, 4*(1), 17-18.**

The article states that TMS of the medial-frontal cortex impairs processing of angry facial expressions but not happy expressions. Following TMS, subjects were slower to respond correctly to anger and quicker to respond to happiness. There was no difference between parietal

and medial frontal stimulation. The article concluded that separate neural systems are involved in the recognition of different emotions from facial expression.

9. Terney, D., Chaieb, L., Moliadze, V., Antal, A., & Paulus, W. (2008). Increasing human brain excitability by transcranial high-frequency random noise stimulation. *The Journal of Neuroscience*, *28*(52), 14147-14155.

The article provides evidence that there is increased motor excitability with tRNS (transcranial high frequency random noise stimulation). Weak tRNS over M1 enhances corticospinal excitability both during and after stimulation in the healthy human brain. High frequency subdivision of the whole tRNS spectrum between 100 and 640 Hz is functionally responsible for inducing excitability in the M1. Externally induced neuronal plasticity is highly dependent on the state of the subject during stimulation. tRNS-driven cortical excitability change facilitates the learning process. High bone resistance is the reason why TMS replaced pulsed electrical stimulation in 1985 to avoid pain. tDCS produces excitation at one electrode and induces inhibition at the other while tRNS produces only excitatory aftereffects. The main advantage of this seems to be the direction of insensitivity of the stimulation.

10. Gandiga, P.C., Hummel, F.C., & Cohen, L.G. (2006). Transcranial dc stimulation (tDCS): a tool for double-blind sham-controlled clinical studies in brain stimulation. *Clinical Neurophysiology*, *117*, 846-850.

The article states that tDCS is safe in both healthy and stroke patients. Patients could not tell the difference between sham and tDCS, therefore it is a great method to use for a double blind study in neurorehabilitation and cognitive neuroscience.

11. Boggio, P.S., Ferrucci, R., Rigonatti, S.P., Covre, P., Nitsche, M., Pascual-Leone, A., & Fregni, F. (2006). Effects of transcranial direct current stimulation on working memory in patients with Parkinson's disease. *Journal of the Neurological Sciences*, *249*, 31-38.

This article discusses the beneficial effect of tDCS on working memory. Selectively anodal tDCS of the left dorsolateral prefrontal cortex (LDLPFC) improved accuracy but not speed of movement. Age may contribute to necessity for higher tDCS. Dopamine has an important role in working memory generation and formation. Amphetamine enhances working memory and increases brain activity in prefrontal cortex in healthy subjects. Left prefrontal cortex anodal stimulation with 2 mA has a potential positive impact on working memory in patients with Parkinsons.

12. Been, G., Ngo, T.T., Miller, S.M., & Fitsgerald, P.B. (2007). The use of tDCS and CVS as methods of non-invasive brain stimulation. *Brain Research Reviews*, *56*, 346-361.

The article covers Caloric Vestibular Stimulation (CVS) – CVS is a safe, non-invasive, and inexpensive unilateral hemispheric activation. tDCS and CVS have shown that they may have therapeutic potential in cognitive neuroscience disorders. Both have been proven to be very safe and are being investigated more for their ability to selectively modulate cortical excitability and

induce relative unihemispheric activation. Both methods are also relatively free of side effects and cheaper than rTMS.

13. Antal, A., Nitsche, M.A., & Paulus, W. (2006). Transcranial direct current stimulation and the visual cortex. *Brain Research Bulletin*, *68*, 459-463.

This article says that anodal tDCS applied to the surface of both the motor and the visual cortex increased cortical excitability and activity by depolarizing neuronal membranes and subthreshold level. Cathodal tDCS resulted in the opposite effect.

14. Bolte, S., & Poustka, F. (2004). Comparing the intelligence profiles of savant and nonsavant individuals with autistic disorder. *Intelligence*, *32*, 121-131.

The article provides evidence that autistic savant and nonsavant individuals did not differ significantly in their general intellectual level. Autistic savants performed better on the Digit Span test than nonsavants. There are only minor differences in intelligence profile between autistic individuals with and without savant talents. The superiority of savants on the digit test may suggest less impaired working memory and executive function.

15. Snyder, A.W., Mulcahy, E., Taylor, J.L., Mitchell, D.J., Sachdev, P., & Gandevia, S.C. (2003). Savant-like skills exposed in normal people by suppressing the left front fronto-temporal lobe. *Journal of Integrative Neuroscience*, *2*(2), 149-158.

The article discusses artistic performance changes with TMS. Low frequency TMS of the left fronto-temporal lobe does not lead to a systematic improvement of artistic performance, but caused major changes in drawing scheme or convention in 4 of 11 participants. These effects are due to turning off part of the brain with TMS, not exciting it. Savant-like skills can be facilitated in a healthy person by suppressing part of the brain with TMS.

16. Poreisz, C., Boros, K., Antal, A., & Paulus, W. (2007). Safety aspects of transcranial direct current stimulation concerning healthy subjects and patients. *Brain Research Bulletin*, *72*, 208-214.

Following current tDCS guidelines, there are only relatively minor adverse effects. Only 16.7% of patients felt a difference between cathodal, anodal, and sham stimulation. tDCS is associated with itching, tingling, burning, and pain under the electrodes. The applicability of tDCS is not restricted to the motor cortex, as it has been shown to be effective in visual, prefrontal, somatosensory, and temportal cortices.

17. Carey, J.R., Fregni, F., & Pascual-Leone, A. (2006). rTMS combined with motor learning training in healthy subjects. *Restorative Neurology and Neuroscience*, *24*, 191-199.

The article discusses motor learning ability differences with and without rTMS. The performance of subjects receiving active rTMS did not improve during training, whereas sham rTMS subjects‘ performance did improve. The effect was not apparent at the first posttest but

appeared at every posttest afterwards up to 12 minutes after the rTMS was stopped. After 12 minutes of rTMS the interference disappeared and the test group didn‘t differ from the control group.

18. Rossi, S., Cappa, S., Babiloni, C., Pasqualetti, P., Miniussi, C., Carducci, F., Babiloni, F., & Rossini, P.M. (2001). Prefrontal cortex in long-term memory: an "interference" approach using magnetic stimulation. *Nature Neuroscience*, *4*(9), 948-1017.

This article discusses the role of the prefrontal cortex in long-term memory formation and retrieval. The right dorsolateral prefrontal cortex is crucial for the retrieval of encoded pictorial information, and the left DLPFC is involved in the encoding of pictorial information. Bilateral PFC engagement, with left functional prevalence, is associated with encoding of pictorial material memory traces.

19. Fecteau, S., Pascual-Leone, A., Zald, D.H., Liguori, Theoret, H., P., Boggio, P.S., & Fregni, F. (2007). Activation of prefrontal cortex by transcranial direct current stimulation reduces appetite for risk during ambiguous decision making. *The Journal of Neuroscience*, *27*(23), 6212-6218.

The article discusses how tDCS can alter the appetite for risk. Participants receiving bilateral DLPFC tDCS with an anodal electrode over the right or left DLPFC displayed a conservative, risk-averse response style, making fewer pumps on the BART (balloon analogous risk task) than those with sham stimulation and those with unilateral DLPFC stimulation. This can be used as a treatment method for those with an addiction as those people show excessively risky decision making. Imaging studies have shown abnormal activity in the PFC, including the DLPFC, in individuals with nicotine, drug, and food craving addictions.

20. Rami, L., Gironell, A., Kulisevsky, J., Garcia-Sanchez, C., Berthier, M., & Esteves-Gonzalez, A. (2003). Effects of repetitive transcranial magnetic stimulation on memory subtypes: a controlled study. *Neuropsychologia*, *41*, 1877-1883.

High frequency rTMS over the left DLPFC disrupts performance in the verbal episodic memory in healthy right-handed men. This would suggest that rTMS over the left DLPFC blocked one of the targeted brain areas in the new verbal episodic learning. High frequency rTMS parameters provoked a direct or indirect blockade of some brain areas implicated in the episodic memory located in the left DLPFC. rTMS effects of cognitive function may depend on timing of rTMS application rather than the stimulation parameters. There is a strong correlation between transitory disruption of left DLPFC and verbal episodic memory performance.

21. Hecht, D., Walsh, V., & Lavidor, M. (2010). Transcranial direct current stimulation facilitates decision. *The Journal of Neuroscience*, *30*(12), 4241-4245.

This article states that anodal tDCS stimulation of the brain leads to behavioral enhancement or a change in bias. Participants were given a sequence of binary events where one event occurs more often than the other. The LH will look at the previous events and try to find a pattern to make an educated guess at the next event. The right side of the brain will always choose the

event that shows up more often. When anodal tDCS is applied over the LH, participants were quicker to choose the more frequent event although there was no overall difference in guessing strategy in any of the 3 groups (RH anodal/LH cathodal, LH anodal/RH cathodal, no tDCS).

22. Floel, A., Rosser, N., Michka, O., Knecht, S., & Breitenstein, C. (2008). Noninvasive brain stimulation improves language learning. *Journal of Cognitive Neuroscience*, *20*(8), 1415-1422.

This article states that anodal tDCS to the LH significantly improves acquisition of a novel vocabulary in healthy people. This would suggest that, with tDCS and proper training, language learning can be improved significantly in people with chronic aphasia after brain lesion also. These effects are thought to be a result of an improved ability to recognize correct word pairings and reject incorrect pairings. Other evidence suggests that the performance improvement was not a result of increased neuronal sensitivity within a sensory pathway.

23. Schutter, D. J.L.G., Hofman, D., & VanHonk, J. (2008). Fearful faces selectively increase corticospinal motor tract excitability: a transcranial magnetic stimulation study. *Psychophysiology*, *45*, 345-348.

This study produced the first direct evidence for selective increases in corticospinal motor tract excitability to fearful facial expressions. Selective attenuation to fearful facial expressions can be attenuated by reducing frontal cortical excitability with slow frequency rTMS.

24. Snyder, A. (2009). Explaining and inducing savant skills: privileged access to lower level, less-processed information. *Philosophical Transactions of the Royal Society*, *364*, 1399-1405.

This article states that inhibitory rTMS of the left anterior temporal lobe is thought to enable savant like skills. It is thought that savant skills are facilitated by privileged access to raw, less-processed sensory information, information that exists in all brains but is inaccessible owing to top-down inhibition. There was nothing proven in this paper, but many hypotheses leading to future research were made.

25. Hajcak, G., Molnar, C., George, M, Bolger, K., Koola, J., & Nahas, Z. (2007). Emotion facilitates action: a transcranial magnetic stimulation study of motor cortex excitability during picture viewing. *Psychophysiology*, *44*, 91-97.

This article explains that MEP (Motor Evoked Potential) amplitude varies as a function of emotional stimuli. MEP amplitudes were larger after TMS when participants viewed pleasant pictures rather than neutral ones. This was not true before TMS which suggests that TMS increases excitability in the targeted region.

26. Dockery, C.A., Hueckel-Weng, R., Birbaumer, N., & Plewnia, C. (2009). Enhancement of planning ability by transcranial direct current stimulation. *The Journal of Neuroscience*, *29*(22), 7271-7277.

Unlike TMS, anodal and cathodal tDCS enhance planning ability (shown by the Tower of London (TOL) test). Polarity-specific effects are more pronounced at higher task load levels and sustained for up to a year without further tDCS application. Females showed greater recruitment of the DLPFC than males in TOL BOLD activation patterns.

27. Osaka, N., Otsuka, Y., Hirose, N., Ikeda, T., Mima, T., Fukuyama, H., & Osaka, M. (2007). Transcranial magnetic stimulation (TMS) applied to left dorsolateral prefrontal cortex disrupts verbal working memory performance in humans. *Neuroscience Letters*, *418*, 232-235.

TMS stimulation to the LDLPFC applied immediately after the reading spat test sentences interferes with the rehearsal involved in maintaining the target word and deteriorates performance. The executive system in the LDLPFC has crucial contribution to working memory during sentence comprehension.

28. Fregni, F., Boggio, P.S., Nitsche, M., Bermpohl, F., Antal, A., Feredoes, E., Marcolin, M.A., …Pascual-Leone, A. (2005). Anodal transcranial direct current stimulation of prefrontal cortex enhances working memory. *Experimental Brain Research*, *166*, 23-30.

Anodal stimulation of the left prefrontal area increases accuracy task performance. TMS had the opposite effect, and creates virtual lesion by transiently disrupting brain activity. In a sequential-letter-matching task, anodal tDCS of the LPFC enhances working memory performance.

29. Fregni, F., Boggio, P., Nitche, M, Rigonatti, S., & Pascual-Leone, A. (2006). Cognitive effects of repeated sessions of transcranial direct current stimulation in patients with depression. *Depression and Anxiety*, *23*, 482-484.

This article suggests that repeated sessions of tDCS do not produce cognitive impairment in patients with major depression. However, tDCS does improve working memory function. There was no correlation between mood improvement and cognitive improvement.

30. Gijsman, H.J., & Cohen, H. (2005). Letter to the editor: mania after transcranial magnetic stimulation. *American Journal of Psychiatry*, *162*(2), 398-400.

This article says that mania is a possible side effect of TMS in patients with PTSD. Due to the fact that mania is not a common symptom with PTSD, its unusually high occurrence rate is more likely to be a side effect of right dorsolateral prefrontal cortex TMS. Negative findings such as this are commonly overlooked when a new and exciting treatment method such as this is discovered.

31. Isogawa, K., Fujiki, M., Akiyoshi, J., Tsutsumi, T., Kodama, K., Matsushita, H., …Kobayashi, H. (2005). Anxiolytic suppression of repetitive transcranial magnetic stimulation-induced anxiety in the rats. *Progress in Neuro-Psychopharmacology*, *29*, 664-668.

This article states that rTMS administered for 10 days caused anxiety in rats which was shown by many behavioral changes compared to the control group. rTMS is also known to cause a decrease in happiness in humans. Drugs such as diazepam, alprazolam, and busipirone reversed the effects of rTMS. Chronic rTMS treatment provides a good animal model for anxiety.

32. Takeuchi, N., Ikoma, K., Chuma, T., & Matsuo, Y. (2006). Measurement of transcallosal inhibition in traumatic brain injury by transcranial magnetic stimulation. *Brain Injury*, *20*(9), 991-996.

There was a significant difference between the control subjects and the patients with a traumatic brain injury (TBI) for the amount of transcallosal inhibition (TCI), but not for the resting motor threshold, the central motor latency time, or amplitude. TCI is positively correlated with the severity of a TBI. An assessment by TCI was found to be more sensitive to detecting abnormal findings than TMS. TBI severity is measured with TCI by testing the functional integrity of the corpus callosum.

33. Burle, B., Bonnet, M., Vidal, F., Possamai, C., & Hasbroucq, T. (2002). A Transcranial magnetic stimulation study of information processing in the motor cortex: relationship between the silent period and the reaction time delay. *Psychphysiology*, *39*, 207-217.

This article studied the effect of TMS on reaction time (RT) and the silent period (SP). At early stimulation times, TMS shortened RT. At later stimulation times TMS had a disruptive effect. When the stimulated cortex was involved in response, there was a correlation between the silent period and the reaction time. SP and RT delay are thought to be caused by the activation of the same inhibitory neurons.

34. Devlin, J.T., & Watkins, K.E. (2007). Stimulating language: insights from TMS. *Brain*, *130*(3), 610-622.

When using rTMS to create virtual lesions, it provides the spatio-temporal accuracy to complement information from imaging and patient studies. This makes TMS an essential tool for studying language at both cognitive and neural levels.

35. Inomata-Terada, S., Furubayashi, T., Ohnishi, T., Moriguchi, Y., Hanajima, R., Terao, Y., & Ugawa, Y. (2008). Hemodynamic changes at the primary motor cortex during. *Japanese Society of Clinical Neurophysiology / Clinical Neurophysiology*, *119*, e75-e93.

The article studied hemodynamic changes in the primary motor cortex during rTMS over the supplementary motor area. Oxyhemoglobin and total hemoglobin concentrations decreased after low frequency stimulation but increased after high frequency stimulation. The low frequency decrease is a result of long-lasting inhibition after the transient facilitation. The high frequency increase may be a result of the summation of transient facilitations overcoming the inhibition.

36. Kito, S., & Kyorin, Y.K. (2008). Changes in regional cerebral blood flow after low-frequency. *Japanese Society of Clinical Neurophysiology / Clinical Neurophysiology*, *119*, e75-e93.

The article focuses on changes in regional cerebral blood flow caused by low-frequency TMS. Subjects with major depressive disorder received the TMS while being observed using SPECT. After TMS scores on the Hamilton Rating Scale for Depression were significantly lower blood-flow to the bilateral prefrontal regions, anterior cingulate, left parietal region, and limbic-paralimbic regions decreased. There was no increase in regional cerebral bloodflow. This suggests that neural pathways in the prefrontal and limbic-paralimbic regions are responsible for the antidepressant effect.

37. Marshall, L., Molle, M., Hallschmid, M., & Born, J. (2004). Transcranial direct current stimulation during sleep improves declarative memory. *The Journal of Neuroscience*, *24*(44), 9985-9992.

tDCS during slow-wave rich non-REM sleep distinctly increases word pair retention. When applied while awake, tDCS had no effect on declarative memory or procedural memory. tDCS increased sleep depth toward the end of the stimulation period. Improved mood was also noted after tDCS when applied during sleep or while awake.

38. McConnell, K.A., Bohning, D.E., Nahas, Z., Shastri, A., Teneback, C., Lorberbaum, J.P., Lomarev, M.P., …George, M.S. (2003). Bold fMRI response to direct stimulation transcranial magnetic. *Journal Neural Transmission*, *110*, 495-507.

This article compares the brain‘s hemodynamic response in elderly healthy adults and gender matched younger adults. The older group showed a significantly increased percent BOLD fMRI signal change. Results suggest that TMS may override age-related physiology differences.

39. McKeefry, D.J., Burton, M.P., Vakrou, C., Barrett, B.T., & Morland, A.B. (2008). Induced deficits in speed perception by transcranial magnetic stimulation of human cortical areas V5/MT+ and V3A. *The Journal of Neuroscience*, *28*(27), 6848-6857.

Human speed perception can be selectively and reversibly impaired with rTMS applied to cortical areas V5/MT+ and V3A. The induced impairment can be both task and location specific and is dependent on the magnitude of the stimulation.

40. Ragert, P., Franzkowiak, S., Schwenkreis, P., Tegenthoff, M., & Dinse, H.R. (2008). Improvement of tactile perception and enhancement of cortical. *Experimental Brain Research*, *184*, 1-11.

This article discusses the intermittent theta burst stimulation – brief period of iTBS applied over the hand representation of left S1 can induce perceptual changes as expressed by an improvement in tactile 2-point discrimination performance on d2 (index finger) of the right hand. Improvement of tactile perception is associated with a disinhibition or hyperexcitability within S1.

41. Ragert, P., Vandermeeren, Y., Camus, M., & Cohen, L.G. (2008). Improvement of spatial tactile acuity by transcranial direct. *Clinical Neurophysiology*, *119*, 805-811.

This paper states that anodal tDCS over the primary somatosensory cortex (S1) results in improvement in tactile spatial acuity in the contralateral hand. It is unknown whether this is a result of tDCS induced excitability changes within S1 or a result of an improved SNR for grating detection in the somatosensory cortices.

42. Rossi, S., & Rossini, P.M. (2004). TMS in cognitive plasticity and the. *TRENDS in Cognitive Sciences*, *8*(6), 273-279.

The article illustrates that TMS is used to interfere with higher order brain functions. The authors posit that TMS may be able to produce a permanent change in synapse efficacy in the area of stimulation.

43. Silvanto, J., Cattaneo, Z., Battelli, L., & Pacual-Leone, A. (2008). Baseline cortical excitability determines whether TMS disrupts. *Journal of Neurophysiology*, *99*, 2725-2730.

Online TMS applied over the motion area V5/MT (middle temporal visual area) can either suppress or facilitate motion detection depending on the initial activation state of the region. TMS during a motion-detection task impaired subject performance. Suppression of V5/MT activity with off-line rTMS impaired subsequent motion detection test performance. Online V5/MT TMS had a facilitatory effect on motion detection with the region that had been previously stimulated with offline rTMS prior to motion-detection test. Behavioral effects of TMS are dependent on the excitability of neurons in the stimulated region, demonstrating the importance of the initial activity state in modulating the efficacy of TMS.

44. Sparing, R., Dafotakis, M., Meister, I.G., Thirugnanasambandam, N., & Fink, G.R. (2008). Enhancing language performance with non-invasive. *Neuropsychologia*, *46*, 261-268.

The article says that anodal tDCS over the left PPR (posterior perisylvian region (an area which includes Wernicke‘s area)) improves naming in aphasics. It is not known, however, what exactly is happening to cause this change.

45. Sparing, R., & Mottaghy, F.M. (2008). Noninvasive brain stimulation with transcranial magnetic or. *Methods*, *44*, 329-337.

This article is a very basic overview of TMS and tDCS. Both stimulation methods have advantages and disadvantages. Both methods look promising for use in future research and therapeutic applications.

46. Jin, Y., & Hilgetag, C.C. (2008). Perturbation of visuospatial attention by high-frequency. *Experimental Brain Research*, *189*, 121-128.

The article says that an increase in metabolic activity in stimulated areas does not result in improved functional processing. Instead, impairment of the detection of contralateral stimuli was observed. This suggests that high-frequency TMS of an injured hemisphere of the brain may lead to further impairment. This cannot be guaranteed because this study was performed on healthy patients, not injured ones.

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Acronym List

ACC	Anterior cingulate cortex
ACG	Anterior cingulate gyrus
ADHD	Attention deficit hyperactivity disorder
AFRL	Air Force Research Laboratory
AI	Anterior insula
ARL	Army Research Laboratory
BART	Balloon analogous risk task
BDNF	Brain-derived neurotrophic factor
BOLD	Blood oxygenation level-dependent
CA3	Cornu Ammonis region 3
CBF	Cerebral blood flow
CBFV	Cerebral blood flow velocity
COMT	Catechol-O-methyltransferase
CPT	Continuous performance task
CRH	Corticotropin releasing hormone
CRHR1	Corticotropin releasing hormone receptor 1
CVS	Caloric vestibular stimulation
d2	Right and left index fingers
DARPA	Defense Advanced Research Projects Agency
DC	Direct current
DLPFC	Dorsolateral prefrontal cortex
DoD	Department of Defense
DSI	Diffusion spectrum imaging

EEG	Electroencephalography
FKBP5	FK506 binding protein 5
fMRI	Functional Magnetic Resonance Imaging
GABA	Gamma-Aminobutyric acid
GCs	Glucocorticoids
GNG	Go/NoGo
GR	Glucocorticoid receptor
HPA	Hypothalamic pituitary axis
Hz	Hertz
hyperMRI	Hyperfunctional magnetic resonance imaging
IARPA	Intelligence Advanced Research Projects Activity
iTBS	intermittent theta burst stimulation
LDLPFC	Left dorsolateral prefrontal cortex
LDV	Laser doppler vibrometry
LH	Left hemisphere
LTP	Long-term potentiation
MAOA	Monoamine oxidase A
MCAs	Middle cerebral arteries
MEG	Magnetoencephalography
MEP	Motor evoked potential
MWM	Morris Water Maze
mA	milliampere
NIH	National Institute of Health
NIRS	Near-infrared spectroscopy
NPY	Neuropeptide Y

OEF	Operation Enduring Freedom
OFC	Orbitofrontal cortex
OIF	Operation Iraqi Freedom
PcC	Paracingulate cortex
PFC	Prefrontal cortex
PPR	Posterior perisylvian region
PTSD	Post-traumatic stress disorder
REM	Rapid eye movement
RH	Right hemisphere
RT	Reaction time
rCBF	regional cerebral blood flow
rTMS	repetitive transcranial magnetic stimulation
S1	Somatosensory cortex
SA	Septal area
SARTs	Sustained attention to response tasks
SLC6A4	Solute carrier family 6, member 4
SNS	Sympathetic nervous system
SOs	Slow oscillations
SP	Silent period
SPECT	Single-photon emission computed tomography
sec	seconds
T1	Time 1
T2	Time 2
TBI	Traumatic brain injury

TCI	Transcallosal inhibition
TDCS	Transcranial direct current stimulation
TMS	Transcranial magnetic stimulation
TMT	Tympanic membrane temperature
TOL	Tower of London
tRNS	transcranial high frequency random noise stimulation
U.S.	United States
V3A	Visual complex 3A, extrastriate visual cortex
V5/MT+	Visual area 5/medial temporal cortex
VTA	Ventral tegmental area